Access DB# L4931

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: R. Gerstl Examiner #: 59972 Date: 2/22/02

Art Unit: 1626 Phone Number 30[illegible] 4931 Serial Number: 67702

Mail Box and Bldg/Room Location: ~~7B09~~ 3D19 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

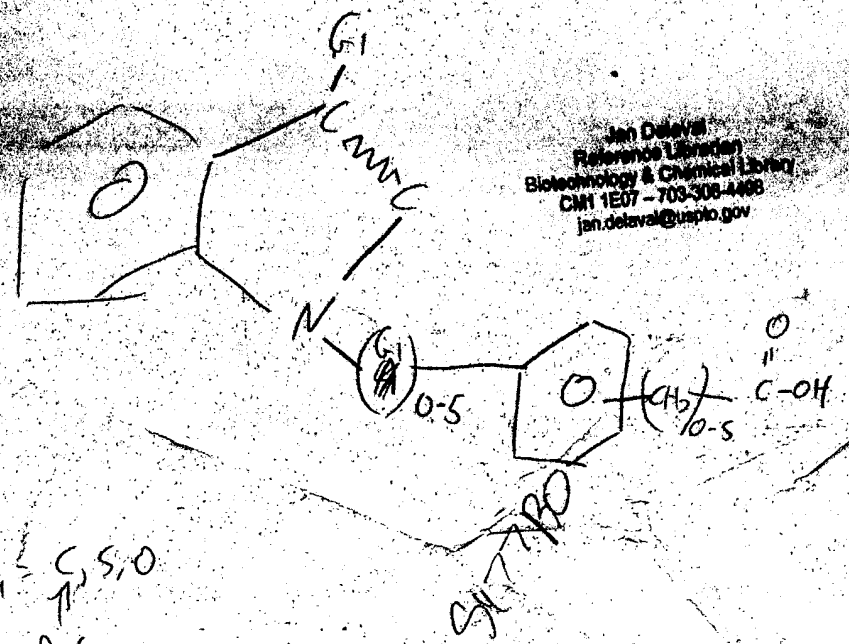
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention:

Inventors (please provide full names):

Earliest Priority Filing Date:

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4468
jan.delaval@uspto.gov

G1 ≠ C,S,O

f.c

****

STAFF USE ONLY

Searcher: [illegible]

Searcher Phone #: 4458

Searcher Location:

Date Searcher Picked Up: 4/22/02

Date Completed: 4/22/02

Searcher Prep & Review Time:

Clerical Prep Time: 10

Online Time: 25

Type of Search

NA Sequence (#)

AA Sequence (#)

Structure (#) ✓

Bibliographic

Litigation

Fulltext

Patent Family

Other

Vendors and cost where applicable

STN ✓

Dialog

Questel/Orbit

Dr.Link

Lexis/Nexis

Sequence Systems

WWW/Internet

Other (specify)

PTO-1590 (8-01)

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FILE 'REGISTRY' ENTERED AT 14:58:52 ON 22 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:   21 APR 2002  HIGHEST RN 406458-32-0
DICTIONARY FILE UPDATES:  21 APR 2002  HIGHEST RN 406458-32-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d sta que l5
L1                STR
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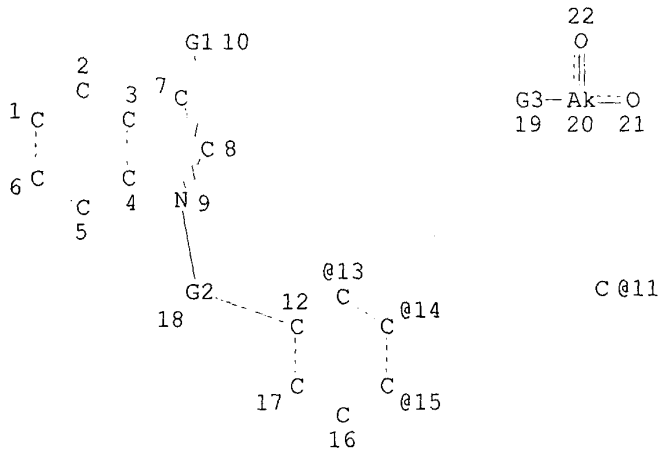


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REP G2=(0-1) AK
VAR G3=13/14/15
NODE ATTRIBUTES:
NSPEC   IS RC     AT  11
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
L3       329075 SEA FILE=REGISTRY ABB=ON  PLU=ON  46.150.18/RID AND NC4-C6/ES
L5          353 SEA FILE=REGISTRY SUB=L3 SSS FUL L1

100.0% PROCESSED 306395 ITERATIONS                      353 ANSWERS
SEARCH TIME: 00.00.21
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Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

256413

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=> d his l5-

     (FILE 'REGISTRY' ENTERED AT 14:40:04 ON 22 APR 2002)
L5          353 S L1 FUL SUB=L3
                SAV L5 GERSTL677/A

     FILE 'HCAOLD' ENTERED AT 14:45:00 ON 22 APR 2002
L6            7 S L5
                SEL AN
                EDIT /AN /OREF

     FILE 'HCAPLUS' ENTERED AT 14:45:38 ON 22 APR 2002
L7           14 S E1-E7
                SEL DN AN 1 4 6 8 10 12 14
L8            7 S L7 NOT E8-E28
L9           83 S L5
                E SEEHRA J/AU
L10          32 S E3-E6
                E KAILA N/AU
L11          20 S E3,E4
                E MCKEW J/AU
L12          10 S E4-E6
                E MC KEW J/AU
                E LOVERING F/AU
L13          10 S E4-E6
                E BEMIS J/AU
L14           7 S E8,E9
                E XIANG Y/AU
L15          37 S E3-E8
L16          27 S E33-E35
L17           9 S E39
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L18        2811 S (AM? HOME PROD?)/PA,CS
L19         308 S AMP/PA,CS
L20         666 S A M P/PA,CS
L21           0 S (GENETIC# INS)/PA,CS
L22        2712 S (GENETIC# INST)/PA,CS
L23       16037 S (GENETIC# INSTITUTE?)/PA,CS
L24           5 S L9 AND L10-L23
L25          60 S L9 AND (PD<=19980225 OR PRD<=19980225 OR AD<=19980225)

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L27           1 S E48
L28           1 S E83
                E PHOSPHOLIPASE
L29        1821 S E3
L30        1819 S L29 NOT L26-L28

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L32       13422 S L30
L33       36159 S PHOSPHOLIPASE
L34        3705 S PLA2
L35           7 S L25 AND L31-L34
L36          42 S L25 AND P/DT
L37          21 S L25 AND US/PC
L38          35 S (1 OR 63)/SC,SX AND L25
L39          25 S L38 AND L36
L40          16 S L37 AND L39
L41          21 S L24,L35,L40
L42           5 S L37 NOT L41
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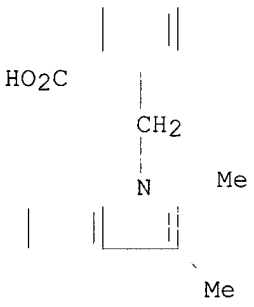
SEL HIT RN L41

FILE 'REGISTRY' ENTERED AT 14:57:42 ON 22 APR 2002
L43 143 S E1-E143
L44 8 S L5 AND CAOLD/LC
L45 151 S L43,L44

FILE 'REGISTRY' ENTERED AT 14:58:52 ON 22 APR 2002

=> d ide can tot l44

L44 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 132725-42-9 REGISTRY
CN o-Toluic acid, .alpha.-2,3-dimethylindol-1-yl- (6CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H17 N O2
SR CAOLD
LC STN Files: CAOLD

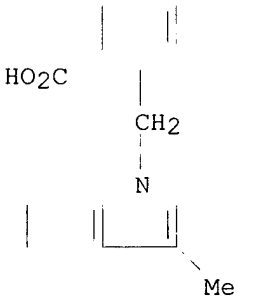


Hits for CAOLD references

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

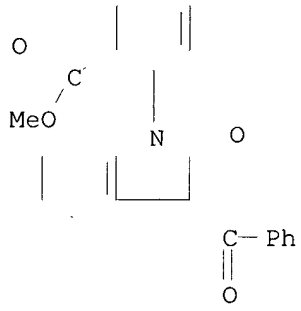
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L44 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 108973-42-8 REGISTRY
CN o-Toluic acid, .alpha.-3-methylindol-1-yl- (6CI) (CA INDEX NAME)
FS 3D CONCORD
MF C17 H15 N O2
SR CAOLD
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

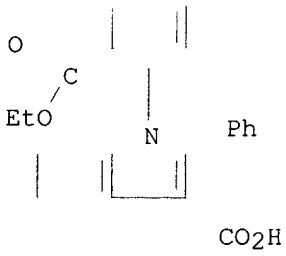
L44 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 3549-84-6 REGISTRY
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)-, methyl ester (6CI, 7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H17 N O4
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L44 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 3547-22-6 REGISTRY
CN Indole-3-carboxylic acid, 1-(o-carboxyphenyl)-2-phenyl-, 1-ethyl ester (7CI, 8CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Indole-3-carboxylic acid, 1-(o-carboxyphenyl)-2-phenyl-, o-ethyl ester (6CI)
FS 3D CONCORD
MF C24 H19 N O4
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)

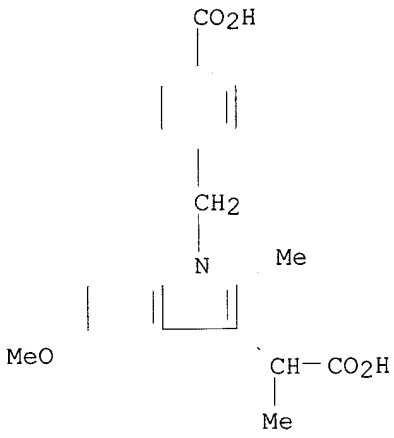


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L44 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 3447-34-5 REGISTRY

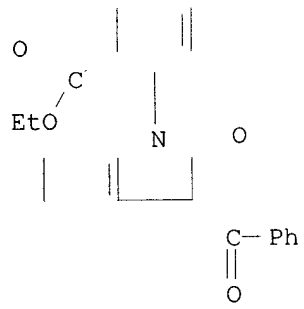
CN Indole-3-acetic acid, 1-(p-carboxybenzyl)-5-methoxy-.alpha.,2-dimethyl- (7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H21 N O5
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L44 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 3283-85-0 REGISTRY
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)-, ethyl ester (6CI, 7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H19 N O4
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)

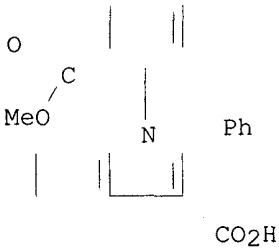


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L44 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 3283-77-0 REGISTRY
CN Indole-3-carboxylic acid, 1-(o-carboxyphenyl)-2-phenyl-, 1-methyl ester

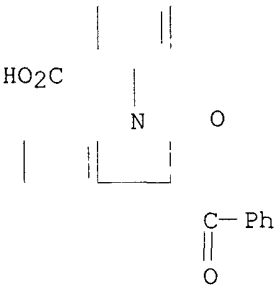
(7CI, 8CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Indole-3-carboxylic acid, 1-(o-carboxyphenyl)-2-phenyl-, o-methyl ester (6CI)
FS 3D CONCORD
MF C23 H17 N O4
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L44 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2002 ACS
RN 3283-76-9 REGISTRY
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)- (6CI, 7CI, 8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H15 N O4
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> fil hcaold
FILE 'HCAOLD' ENTERED AT 14:59:14 ON 22 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

PRE-1967 CHEMICAL ABSTRACTS FILE WITH HOUR-BASED PRICING

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d all hitstr tot 16

L6 ANSWER 1 OF 7 HCAOLD COPYRIGHT 2002 ACS
AN CA65:3843e CAOLD
TI 7-(diphenylmethyl)-7-hydroxy-2,3-norbornane-dicarboxylic acid .gamma.-lactones (isomeric)
PA McNeil Laboratories, Inc.
DT Patent
TI isomeric 7-(diphenylmethyl)-7-hydroxy-2,3-norbornanedicarboxylic acid .gamma.-lactones
AU Poos, George I.
DT Patent
TI .alpha.-(1-benzyl-3-indolyl)alkanecarboxylic acids
AU Sarett, Lewis H.; Shen, T. Y.
PA Merck & Co., Inc.
DT Patent

	PATENT NO.	KIND	DATE		
PI	US 3242163		1966		
	NL 6513089				
PI	US 3250789		1966		

for Abstracts see pages 16 - 28

IT	349-95-1	455-19-6	874-87-3	939-99-1	1	
	1140-47-2	1208-87-3	1583-83-1	1703-96-4	1	
	2175-90-8	2320-32-3	3446-61-5	3446-65-9	3	
	3446-69-3	3446-75-1	3446-77-3	3446-79-5	3	
	3446-82-0	3446-83-1	3446-86-4	3446-91-1	3	
	3447-16-3	3447-17-4	3447-18-5	3447-19-6	3447-20-9	3447-21-0
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	94004-67-8	95223-38-4	95291-44-4	95319-44-1	95319-54-3	95320-49-3
	95437-55-1	95822-68-7	96309-57-8	96367-30-5	96467-96-8	96585-34-1

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all tot l8

L8 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1966:420746
DN 65:20746
OREF 65:**3843e**
TI .alpha.-(1-Be rboxylic acids
IN Sarett, Lewis
PA Merck & Co. I
SO 19 pp.
DT Patent
LA Unavailable
NCL 260211000
CC 37 (Heterocyclic Compounds (ro Atom))
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3242163		19660322	US	19610313
NL 6513089			NL	

AB Identical with U.S. 3,242,193 (preceding abstr.), except that the claims for R4 are limited to CN, CO2H, and carbalkoxy.

L8 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1966:420745 HCAPLUS
DN 65:20745
OREF 65:**3840e-h,3841a-h,3842a-h,3843a-e**
TI .alpha.-(1-Benzyl-3-indolyl)alkanecarboxylic acids
IN Sarett, Lewis H.; Shen, Tsung-Ying
PA Merck & Co. Inc.
SO 20 pp.
DT Patent
LA Unavailable
NCL 260319000
CC 37 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3242193		19660322	US	19641021

GI For diagram(s), see printed CA Issue.
AB Division of U.S. 3,196,162 (CA 63, 16308a). Cf. following abstr. The reaction in alc. HCl solns. of R4C6H4NHNH2 and R2COCH2CHR3CO2Y give II. The title compds. (I) are prepd. by treatment of II with NaH or other metalating agents, followed by R5bC6H5-bCHR1X. Addn. of 100 g. p-MeC6H4SH in 250 ml. (MeOCH2)2 during 2 hrs. to 41.5 g. 50% NaH dispersion in mineral oil in (MeOCH2)2 at -5 to 0.degree., followed by addn. of 20 ml. Me3COH and stirring 15 min. at 0.degree., then bubbling CHF2Cl through the mixt. 45 min. at -2 to 0.degree., and standing 14 hrs. gave 112.3 g. p-MeC6H4SCHF2 (III), b0.35 32-4.degree., n23D 1.5092. One mole p-MeC6H4OH was similarly converted to 18.5 g. p-MeC6H4OCHF2 (IV), m. 165-7.degree.. Treatment of 8.7 g. III with 8.9 g. (CH2CO)2NBr in 400 ml. CCl4 under irradiation by a 275-watt sun lamp 2 hrs. gave 7.0 g. p-CHF2SC6H4CH2Br (IVa), b0.3 74.degree., n22D 1.5622. IV (14.6 g.) and 16.4 g. (CH2CO)2NBr in 800 ml. CCl4 gave 18.5 g. p-HF2COC6H4CH2Br (V), b0.2 50-52.degree., n23D 1.5170. Treatment of 59.7 g. p-MeC6H4SO2NMe2 with 53.4 g. (CH2CO)2NBr in 500 ml. refluxing CCl4 2.5 hrs. gave p-(Me2N SO2)C6H4CH2Br (VI), m. 85-108.degree. (Skellysolve B). MeSPh (120 g.) and 69 g. MeOCH2Cl in 600 ml. HOAc kept at 78-80.degree. for 2 days, evapd., and distd. gave 68 g. p-MeSC6H4CH2Cl (VII), b1 99.degree.. MeSH (24 g.) was bubbled into

350 ml. EtOH containing 32.5 g. 86.5% KOH, 1.2 ml. H2O was added, followed by 70.3 g. p-ClC6H4CHO in 150 ml. EtOH, and the mixt. was refluxed 3 hrs. with slow introduction of MeSH, then poured into 500 ml. H2O, and extd. with ClCH2CH2Cl, giving p-MeSC6H4CHO, redn. of which by Al(OCHMe2)3 in Me2CHOH, followed by treatment with SOCl2, also gave VII. Action of 82 ml. MeOCH2Cl on 177 g EtSPh in 770 ml. HOAc at 75.degree. 48 hrs. gave p-EtSC6H4CH2Cl (VII), b0.025-0.04 92-102.degree.. Similar treatment of 100 ml. Ph2S with 36.3 ml. MeOCH2Cl in 340 ml. HOAc gave 32 g. of a distillate, b0.005 85-145.degree., which contained 39% p-PhSC6H4CH2Cl (IX). A soln. of 25 g. p-H2NC6H4CH2OH in 200 ml. H2O and 80 ml. HCl at 0-5.degree. was treated with 15.5 g. NaNO2 in 40 ml. H2O and neutralized with KOAc. The cold, neutral soln. was filtered into a soln. of 97.6 g. EtOCS2K in 1000 ml. H2O at 75-80.degree., and the mixt. was heated 1 hr. on a steam bath, cooled, and extd. with 3 250-ml. portions Et2O. The exts. were washed thrice with 250 ml. portions H2O, dried, and evapd. To the residual red oil was added 33 g. KOH in 300 ml. EtOH, the mixt. was refluxed 2 hrs. under N, 50.6 g. PhCH2Cl was added, and refluxing continued 3 hrs. to give p-PhCH2SC6H4CH3OH (XI), m. 75-81.degree. (4:35 C6H6-cyclohexane). Action of 100 ml. SOCl2 on 10.7 g. X at 0.degree. 1 hr. gave p-PhCH2SC6H4CH2Cl, m. 91-3.degree. (EtOH). To 7.92 g. Mg in 50 ml. Et2O was added 10 ml. of a soln. of 61 g. p-F3CC6H4Br in 60 ml. Et2O, followed by 2 ml. MeMgI soln. under N. After initiation of the reaction, 200 ml. Et2O and the rest of the p-F3CC6H4Br soln. were added during 1 hr. After refluxing 1.5 hrs., the soln. was cooled to 5.degree. and 81 g. PhNMeCHO was added over 20 min. After 2 hrs. in an ice bath and 18 hrs. at room temp., the mixt. was treated with 200 ml. 5N H2SO4 with cooling, giving p-F3CC6H4CHO (XI), b12 64.degree., n22D 1.4633. Redn. of 20.9 g. XI with 2.5 g. NaBH4 in 100 ml. C6H6, and treatment with 14 g. SOCl2, gave p-F3CC6H4CH2Cl, b12 68.degree., n22D 1.4622. Mixing 53.3 g. p-H2NC6H4SH in 200 ml. EtOH and 60.2 g. p-ClC6H4CHO in 200 ml. EtOH gave, in 20 min., 97 g. p-ClC6H4CH:NC6H4SH-p (XII). Treatment of 58.2 g. XII with 11.52 g. NaH in 400 ml. Me2NCHO during 2 hrs., then addn. of 35 g. MeI in 100 ml. Me2NCHO during 1 hr., and diln. with 2l. H2O, gave p-ClC6H4CH:NC6H4SMe-p, 12 g. of which was reduced by 4.0 g. NaBH4 in 300 ml. MeOH to give p-ClC6H4CH2NHC6H4SMe-p (XIII). Nitrosation of XIII gave the N-nitroso deriv., redn. of 38 g. of which by Al amalgam in Me2CHOH gave p-ClC6H4N(NH2)C6H4SMe-p; hydrochloride (XIIIa) m. 140.5.degree. (EtOH). A soln. of 44 g. p-MeOC6H4NHNH2.HCl (XIV), 42 g. p-O2NC6H4CH2Cl, and 80 g. Et3N in 500 ml. EtOH was refluxed 6 hrs., and 70 ml. 3.2N HCl in EtOH was added, giving 14.4 g. p-MeOC6H4N(NH2)CH2C6H4NO2-p.HCl (XV), m. 147-50.degree.. Hydrogenation of 37 g. p-MeOC6H4NH2 and 50 g. 2,4-(MeO)2C6H3CHO in 250 ml. EtOH on Ni at 40 psi. gave 2,4-(MeO)2C6H3NHC6H4OMe-p, m. 126-7.degree. (Et2O-EtOH), which on nitrosation and redn. by Al amalgam gave 2,4-(MeO)2C6H3N(NH2)C6H4OMe-p.HCl (XVI), m. 136-9.degree.. A soln. of 25 g. XIV and 20 g. AcCH2CHMeCO2Et (XVII) in 250 ml. 2N alc. HCl, refluxed 30 min. after subsidence of the initial reaction, concd. to 80 ml., dild. with 400 ml. H2O, extd. with Et2O, and the dried exts. evapd. and chromatographed on acid-washed Al2O3 in Et2O-petroleum ether gave II (R2 = R3 = Me, R4 = MeO, Y = Et) (IIa), b0.25 150-3.degree., m. 53-5.5.degree. (petroleum ether). Saponification of 13 g. IIa in 200 ml. EtOH by 20 ml. 34% NaOH 6 hrs. under N, diln. with H2O and acidification gave the free acid (IIb), m. 163-5.degree. (aq. EtOH). Other examples of II similarly prepd. were: IIc (R2 = R3 = Me, R4 = Me, Y = Et), m. 88-8.5.degree. (petroleum ether), from 20 g. p-MeC6H4NHNH2.HCl and 20 g. XVII in 250 ml. 2N alc. HCl; IId (R2 = R3 = H, R4 = MeO, Y = Et), from 0.1 mole each of XIV and (MeO)2CHCH2CH2CO2Et; and IIe (R2 = Me, R3 = H, R4 = Cl, Y = Et), m. 85.degree. (petroleum ether), from 0.1 mole each of AcCH2CH2CO2Et and p- ClC6H4NHNH2.HCl in 300 ml. 2N alc. HCl, refluxed 1 hr. AcCH2CHEtCO2Et was treated with XIV to give II (R2 = Me, Y = Et, R4 = MeO) (IIf). Fused ZnCl2 (28 g.) and 10 g. p-O2NC6H4NHN:CMeCH2CHMeCO2H in 20 ml. abs. EtOH were refluxed under N 12 hrs., dild. with 200 ml. 2.5N HCl, and extd. thrice with 200 ml. Et2O. After drying and concn., the exts. were treated 8 hrs. with 200 ml.

refluxing 1N alc. HCl, concd. to give II (R2 = R3 = Me, R4 = NO2, Y = Et) (IIg). A mixt. of 50 g. 2,4-Me2C6H3NHCOEt, 50 g. NaNH2, and 500 ml. PhNEt2 was refluxed under N 1 hr., to give 38 g. 2-ethyl-5-methylindole (XVII), m. 72-84.degree. (cyclohexane). Treatment of 4.4 g. XVII with 5.4 ml. 25% aq. Me2NH, 2.25 ml. 40% aq. CH2O, and 3 ml. HOAc 5 hrs. and addn. of 25 ml. 10% KOH gave a gum which was extd. with Et2O. Extn. of the Et2O soln. with 1.25N HCl, neutralization, reextn. with Et2O, drying, and evapn. gave 2.3 g. 2-ethyl-5-methylgramine, m. 100-3.degree. (cyclohexane), 2 g. of which and 4.0 g. KCN in 32 ml. 80% EtOH, refluxed 68 hrs., neutralized with HCl, concd., dild. with 20 ml. H2O containing 2.3 g. KOH, refluxed 6 hrs., acidified and extd. with Et2O gave 1.0 g. II (R2 = Et, R3 = H, R4 = Me, Y = H) (IIh), m. 137-8.degree. (C6H6). Treatment of 13 g. IIa in 75 ml. Me2NCHO with 2.5 g. NaH-mineral oil dispersion in 100 ml. Me2NCHO 1 hr., followed by 8.0 g. o-ClC6H4CH2Cl 14 hrs. gave I(R1 = H, R2 = R3 = Me, R4 = MeO, R5 = 2-Cl, b = 1, M = EtO) (Ia), m. 118-22.degree. (C6H6-Skellysolve B). Saponification of Ia in 125 ml. EtOH by 20 ml. 34% NaOH gave 8.5 g. free acid, m. 191-2.degree. (C6H6). Other examples of I prepd. from IIa by action of NaH and a benzyl halide were those in which the benzyl groups were: m-ClC6H4CH2, and the free acid, m. 191-2.degree. (EtOAc-Skellysolve B); 2,4-Cl2C6H3CH2, m. 130.degree. (aq. EtOH), and the free acid, m. 184-6.degree.; p-MeOC6H4CH2, sirup, and the free acid, m. 153-3.5.degree. (C6H6-petr. ether); p-FC6H4CH2, and the free acid, m. 164-5.degree. (EtOAc-petr. ether); p-HF2CSC6H4CH2, oil from IVa, and the free acid, m. 132-3.degree. (PhMe); p-HF2COC6H4CH2, oil, 20.9 g. from 13.0 g. IIa and 12 g. V, and the free acid, m. 144-6.degree.; p-ClC6H4CH2, Ib, which was also prepd. from 11.7 g. IIb, 5.0 g. NaH, and 8.8 g. p-ClC6H4CH2Cl, and the free acid, m. 163-5.degree. (C6H6), p-BrC6H4CH2, and the free acid, from p-BrC6H4CH2OSO2Me; p-IC6H4CH2, and the free acid, from p-IC6H4CH2OSO2C6H4Me-p; p-MeSC6H4CH2, Ic, sirup, from VI, and the free acid, m. 170-1.degree. (C6H6-petr. ether); p-(PhCH2S)C6H4CH2, oil from IIa and IX, and the free acid (Id), m. 150-53.degree. (CCl4); p-CF3C6H4CH2, sirup from XI, and the free acid, m. 176-80.degree. (EtOAc- petr. ether); p-NCC6H4CH2, Ie, m. 72.degree. (EtOH), and the free acid, m. 197-200.degree. (EtOAc-petr. ether); p-(Me2NSO2)C6H4CH2, m. 140.degree. (EtOH), from VI, and the free acid, m. 156.5-8.5.degree. (EtOAc-petr. ether); p-EtSC6H4CH2, from VIII, and the free acid, m. 126-33.degree. (2% C6H6 in abs. EtOH); p-PhSC6H4CH2, oil, 42.5 g. from 13.0 g. IIa and 32 g. IX, and the free acid; p-MeSC6H4CHMe and the free acid; and 4-MeS-2-MeC6H3CH2 and the free acid. IIc and p-ClC6H4CH2Cl gave I (R1 = H, R2 = R3 = R4 = Me, R5 = 4-Cl, b = 1, M = EtO) (Ib), m. 89-90.degree., and the free acid (M = OH), m. 185-6.degree.. IIc (24.5 g.) added during 20 min. to 500 ml. Me2NCHO and 6.0 g. NaH, followed by 6.0 g. VII, gave I (R1 = H, R2 = R3 = R4 = Me, R5 = 4-MeS, b = 1, M = EtO), m. 111-13.degree. (Et2O), saponification of 20 g. of which gave 9.6 g. of the free acid, m. 184-7.degree. (ClCH2CH2Cl). From IId were prepd. Et .alpha.-[1-(p-fluorobenzyl)- 5-methoxy-3-indolyl]acetate, and the free acid; and Et .alpha.-[1-(p- chlorobenzyl)-5-methoxy-3-indolyl]acetate, and the free acid, m. 144-8.degree.. IIe and IIf were also converted to their 1-(p-Cl C6H4CH2) derivs. and the corresponding free acids. IIg was converted to I (R1 = H, R2 = R3 = Me, R4 = NO2, R5 = p- MeO, b = 1, M = EtO) (If), which was hydrogenated on Pd-C to the amino compd. (R4 = NH2), from which the Ac, p-ClC6H4CO, and Me2 derivs. were prepd. The corresponding derivs. were prepd. from the free acid obtained by saponificaton of If. Ar-alkylation of 0.05 mole Et .alpha.-(2-methyl-5-methoxy-3-indolyl)-acetate (IIi) with NaH and 0.05 mole p-(PhCH2O)C6H4CH2Cl gave the 1-(p-(PhCH2O)C6H4CH2 deriv., which was saponified to the free acid, hydrogenolysis of which on 10% Pd-C in EtOH gave [1-(p-hydroxybenzyl)-2-methyl-5-methoxy-3-indolyl]acetic acid. Redn. of 18 g. IIi (Y = Me) with 20 g. Sn and 200 ml. 6N HCl under reflux 18 hrs., followed by reesterification with alc. HCl, gave 2.7 g. Et .alpha.-(2-methyl-5-methoxy-2,3-dihydro-3-in- dolyl)acetate, which was aralkylated to prepare the p-ClC6H4CH2, p-MeOC6H4CH2, p-FC6H4CH2, and p-MeSC6H4CH2 derivs., and the

hydrochlorides of the corresponding acids. IIa was similarly reduced to the 2,3-dihydro deriv., which was aralkylated to prepare its p-ClC6H4CH2 and p-MeSC6H4CH2 derivs., and the corresponding hydrochlorides. Aralkylation of 9.3 g. IIi (Y = Me) in 50 ml. tetrahydrofuran (THF) with 3 g. NaH in 100 ml. Me2NCHO and 13 g. p-BrC6H4CHBrMe gave I (R1 = R2 = Me, R4 = M = MeO, R5 = p-Br, b = 1) (Ig), and the free acid. From 12.58 g. IIi (Y = Me) was also prepd. 15 g. of the p-Me SC6H4CH2 deriv., sirup, which was hydrolyzed to the free acid, m. 155-6.5.degree. (EtOH); Et ester m. 94-5.degree. (EtOH). Oxidn. of 10 g. Ic (M = EtO) in Et2O by monoperphthalic acid at -25 to -20.degree., chromatography of the crude product on Al2O3, and hydrolysis of the eluted esters gave .alpha.-[1-(p-methylsulfonylbenzyl)-2-methyl-5-methoxy-3-indolyl]propionic acid, m. 194-6.degree. (EtOAc-EtOH-petroleum ether) and .alpha.-[1-(p-methylsulfinylbenzyl)- 2-methyl-5-methoxy-3-indolyl]propionic acid, m. 98-101.degree. (EtOAc-EtOH-petroleum ether). Heating 8.8 g. Ic (M = OH) and 14 g. urea 1.5 hrs. at 190-200.degree. gave the amide (M = NH2), m. 143-4.degree. (C6H6-petroleum ether). A soln. of 24.9 g. Ic (M = OH) and 9.5 g. (+)-PhCHMeNH2 in 350 ml. boiling EtOH was cooled to 20-25.degree. and kept 90 min., giving the (+)-Ic salt of (+)-PhCHMeNH2, m. 170-72.degree. (EtOH), [.alpha.]22D 38.5.degree. (MeOH), which treated with HCl gave (+)-Ic, m. 118.degree. (5:3 Et2O-C6H6), [.alpha.]22D 62.4.degree. (EtOH). Similar treatment of Ib (M = OH) gave the (+)-Ib salt of (+)-PhCHMeNH2, m. 148-9.degree. (Me2CHOH), [.alpha.] 22D 43.degree. (MeOH), and (+)-Ib, m. 156-7.degree. (1:1 C6H6-pet. ether), [.alpha.]22D 60.degree. (EtOH). The filtrates gave (-)-Ib, m. 153-4.degree. (C6H6-petr. ether), [.alpha.]23D-58.degree. (EtOH). Treatment of 31 g. XIIIa and 16 g. XVII in 400 ml. 7.5N alc. HCl gave 13 g. Et .alpha.-[1-(p-chlorobenzyl)-2-methyl-5-methylthio-3-indolyl]propionate, sirup, saponification of which gave the free acid, m. 154-60.degree. (MeCN). Similar prepns. included: Et .alpha.-[1-(p-chlorobenzyl)-2-phenyl-5-methoxy-3-indolyl]acetate, and the free acid, from p-ClC6H4CH2N(NH2)C6H4OMe-p.HCl (XVIII) and PhCOCH2CH2CO2Et; 1-(p-methylthiobenzyl)-2-trifluoromethyl-5-methoxy-3-indolyl-acetic acid, m. 168-72.degree. (C6H6), from p-MeSC6H4N(NH2)C6H4OMe-p.HCl (XIX) and F3CCOCH2CH2CO2H (Brown, et al., CA 55, 1431c); Et .alpha.-[1-(p-nitrobenzyl)-2-methyl-5-methoxy-3-indolyl]propionate (Ih), m. 102-3.degree. (EtOH), from XV and XVlI and the free acid, m. 188-90.degree. (aq. EtOH); Et [1-(p-methylthiobenzyl)-5-methoxy-3-indolyl]acetate, and the free acid, from XIX and HCOCH2CH2CO2Et (XX); 1-(p-chlorobenzyl)-5-methoxy-3-indolyl-2-acetic acid, m. 146-8.degree., from XVIII and XX; Et .alpha.-[1-(p-chlorobenzyl)-2-benzyl-5-methoxy-3-indolyl]propionate, and the free acid, from XVIII and PhCH2COCH2-CHMeCO2Et; Et .alpha.-[1-(2,4-dimethoxybenzyl)-2-methyl-5-methoxy-3-indolyl]propionate, and the free acid, from XVI and XVII; and [1-(p-chlorobenzyl)-2-carboxy-5-methoxy-3-indolyl]acetic acid (Ii), m. 213-18.degree. (aq. Me2NCHO), from XVIII and HO2CCOCH2CH2CO2H. Hydrogenation of 2.85 g. Ih on Ni at 45-50.degree. in 60 ml. EtOH in the presence of 2.4 ml. 37% CH2O and 5 ml. HOAc gave Et .alpha.-[1-(p-dimethylaminobenzyl)-2-methyl-5-methoxy-3-indolyl]propionate, saponification of which gave the free acid, m. 193-4.degree. (MeOH). Hydrogenation of 4.25 g. Ih on 1 g. Pd-C in 100 ml. Ac2O and 100 ml. HOAc gave Et .alpha.-[1-(p-acetamidobenzyl) - 2 - methyl - 5 - methoxy-3-indolyl] propionate. Saponification of 2 g. Ie by 25 ml. 30% NaOH in 150 ml. EtOH under reflux 18 hrs., and acidification by HCl gave .alpha.-[1-(p-carboxybenzyl)-2-methyl-5-methoxy-3-indolyl]propionic acid, m. 230-4.degree. (HOAc or aq. EtOH). Refluxing a soln. of Ii in Ac2O 2 hrs. gave the anhydride of Ii, m. 205-11.degree., which reacted with abs. EtOH in the presence of 1 equiv. NaOEt at 0.degree. to give the Et ester (Ij), m. 214-16.degree. (aq. MeOH). Heating 5 g. Ij under N 80 min. at 225.degree. gave Et [1-(p-chlorobenzyl)-5-methoxy-3-indolyl]acetate, free acid, m. 146-8.degree. (MeCN-C6H6). Action of SOCl2 in C6H6 on Ij gave the acid chloride, which was reduced by LiAlH(OCMe3)3 in THF to Et [1-(p-chlorobenzyl)-2-formyl-5-methoxy-3-indolyl]acetate (Ik). Redn. of

Ik by NaBH4 gave the lactone of [1-(p-chlorobenzyl)-2-hydroxymethyl-5-methoxy-3-indolyl]acetic acid, which was treated with PhCH2SK in EtOH to give [1-(p-chlorobenzyl)-2-(benzylthiomethyl)-5-methoxy-3-indolyl]acetic acid. A mixt. of 19 g. (COCl)2 in 25 ml. Et2O and 35.7 g. 1-(p-chlorobenzyl)-2-methyl-5-methoxyindole in 900 ml. Et2O was stirred 2 hrs. and filtered. The solid was added to 660 ml. EtOH and treated with 0.12 mole NaOEt 1 hr., then poured into 660 ml. H2O containing 10 ml. HOAc, giving Et .alpha.- [1-(p-chlorobenzyl)-2 -methyl-5 -methoxy-3 -indolyl] oxoacetate (XXI), m. 113.degree. (C6H6-petr. ether). A mixt. of 36.02 g. MePh3P+Br- and 94.36 ml. 1.10N BuLi in 500 ml. dry Et2O was stirred. 1 hr., and 38 g. XXI in 260 ml. C6H6 and 500 ml. Et2O was added. After 1 hr., the mixt. was heated to 65-70.degree. in a pressure flask 5 hrs. The resulting gum was triturated thrice with 500 ml. portions of 33% C6H6 in Et2O. The dried exts. were concd. to a sirup, which was slurried in C6H6 and chromatographed on Al2O3. Elution with 30% Et2O in pert. ether and evapn. gave Et .alpha.-[1-(p-chlorobenzyl)-2-methyl-5-methoxy-3-indolyl]acrylate (XXII), m. 94-5.degree. (petroleum ether), which was saponified to the free acid, m. 187-8.degree. (EtOH). Treatment of 1.8 g. XXII in 10 ml. THF with 4 g. CH2I2, 1.25 g. Zn-Cu, and 0.2 g. iodine in 20 ml. THF with refluxing under N 20 hrs. gave 1.2 g. Et .alpha.-[1-(p-chlorobenzyl)-2-methyl-5-methoxy-3-indolyl]cyclopropanecarboxylate. The free acid, m. 220-4.degree., was obtained by saponification. The title compds. and their nontoxic salts have anti-inflammatory properties.

L8 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1966:403931 HCAPLUS
DN 65:3931
OREF 65:**688d-h,689a-h,690a-h,691a-b**
TI Indolyl aliphatic acids
IN Sarett, Lewis H.; Shen, Tsung-Ying
PA Merck & Co., Inc.
SO 20 pp.
DT Patent
LA Unavailable
NCL 260211000
CC 37 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3242162		19660322	US	19610313

GI For diagram(s), see printed CA Issue.

AB Division of U.S. 3,196,162 (CA 63, 16308a). The title compds. (I) possess antiinflammatory activity, are effective in inhibiting or preventing formation of granuloma tissue and are therefore useful in the treatment of arthritic and dermatological disorders, exhibit anti-pyretic action, and are useful as sun-screening agents. The anti-inflammatory activity resides in the (+) stereoisomer (or D-isomer). A soln. of 25 g. p-MeOC6H4NHNH2.HCl and 20 g. MeCOCH2CH(Me)CO2Et (II) was heated on a steam bath a few min. to initiate an exothermic reaction. Without heating the mixt. was allowed to reflux gently until the reaction subsided, then refluxed 30 min. on a steam bath, and concd. in vacuo to 80 ml. The concentrate was dild. with 400 ml. H2O, extd. with Et2O, and the Et2O soln. worked up to give a sirup which was purified by chromatography over acid-washed alumina and the eluate was distd. in a short-path distn. app. to give III (R = Et, R2 = Me, R3 = Me, R4 = OMe) (IIIa), b0.25 150-3.degree., m. 535.5.degree.. A soln. of 13 g. IIIa in 75 ml. HCONMe2 was added to a stirred suspension of 2.5 g. NaH-mineral oil dispersion (contg. 52 wt.-% NaH) in 100 ml. HCONMe2, stirred 1 hr. at room temp., and treated with 8 g. o-ClC6H4CH2Cl. The mixt. was kept 14 hrs. at room temp., treated with 500 ml. H2O, extd. with Et2O, the Et2O soln. worked up to give a residue which was chromatographed as above to give I (R = Et, R1 = H, R1 = Me, R3 = Me, R4 = MeO, R5 = o-Cl) (Ia), m. 118-22.degree.. A soln. of Ia in 125 ml. EtOH and 20 ml. 34% NaOH was refluxed 3 hrs., kept

3 days at room temp., dild. with 250 ml. H2O, concd. in vacuo to 200 ml., and extd. with Et2O. The aq. layer was sepd. and acidified with 2.5N HCl to give 8.5 g. I (R = R1 = H, R2 = R3 = Me, R4 = MeO, R5 = o-Cl), m. 191-2.degree. (C6H6). The Na, K, Li, Ca, and NH4+ salts of Ia were prepd. by treating Ia with an aq. soln. of the corresponding NH4+, alkali metal, or alk. earth metal carbonate or hydroxide. Following the above procedures, III (R = Et, R2= Me, R3 = H, R4 = MeO) (0.5 mole) was converted to its Na deriv. and the latter was treated with p-PhCH2OC6H4CH2Cl to give I (R = Et, R1 = H, R2 = Me, R3 = H, R4 = MeO, R5 = p-PhCH2O) which was saponified to I(R = R1 = H, R2 = Me, R3 = H, R4 = MeO, R5 = p-PhCH2O) (Ib). Treatment of Ib in EtOH with H in the presence of 10% Pd-C at 40 psi. gave I(R = H, R1 = H, R2 = Me, R3 = H, R4 = MeO, R5 = p-OH). A soln. of 100 g. p-HSC6H4Me in 250 ml. dry MeOCH2CH2OMe (IV) was added dropwise during 2 hrs. to a stirred suspension of 41.5 g. 50% NaH-mineral oil in 100 ml. IV at -5.degree. to 0.degree.. The mixt. was treated with 20 ml. tert-BuOH, stirred 15 min. at 0.degree., and treated with a stream of CHF2Cl 45 min. with stirring at -2.degree. to 0.degree. kept 14 hrs. at room temp., and worked up to give 112.3 g. p-CHF2SC6H4Me (V), b0.25 32-4.degree. n23D 1.5092. A mixt. of 8.7 g. V and 8.9 g. N-bromosuccinimide in 400 ml. CCl4 was irradiated 2 hrs. to give 7.0 g. p-CHF2SC6H4CH2Br, b0.3 74.degree., n22D 1.5625. The following compds. were similarly obtained by the above procedures: pCHF2OC6H4Me, b. 165-7.degree., and p-CHF2OC6H4CH2Br, b0.2 50-2.degree., n23D 1.5170. A mixt. of 13 g. IIIa, 200 ml. MeOH, and 20 ml. 34% NaOH was refluxed 6 hrs. under N to give III (R = H, R2 = Me, R3 = Me, R4 = MeO, R5 = H) (IIIb), m. 163-5.degree.. IIIb was treated with NaH and p-ClC6H4CH2Cl (VI) as above to give Ic (see below). A mixt. of 18 g. IIIa, 20 g. mossy Sn, and 200 ml. 6N HCl was refluxed 18 hrs. to give 2.7 g. VII (R = Et, R2 = Me, R3 = Me, R4 = MeO) (VIIa). VIIa (0.1 mole) was treated with NaH and VI to give VIII (R = Et, R1 = H, R2 = Me, R3 = H, R4 = MeO, R5 = p-Cl) (VIIIa). Hydrolysis of VIIIa as above gave VIII (R = H, R1 = H, R2 = Me, R3 = H, R4 = MeO, R5 = p-Cl). Similarly prepd. was VIII (R = R1 = R2 = R3 = H, R4 = MeO, R5 = MeS). A mixt. of 10 g. p-nitrophenylhydrazone of MeCOCH2CH(Me)CO2H, 28 g. freshly fused ZnCl2, and 20 ml. abs. EtOH was refluxed 12 hrs. under N, dild. with 200 ml. 2.5N HCl, extd. with 3 .times. 200 ml. Et2O, and worked up to give III (R = Et, R2 = Me, R3 = Me, R4 = NO2), (IIIc). IIIc was converted to I (R = Et, R1 = H, R2 = Me, R3 = Me, R4 = NO2, R5 = p-MeO) (Id). Id (0.05 mole) in 200 ml. EtOH was hydrogenated in the presence of 250 mg. 10% Pd-on-C at 40 psi. at room temp. to give I (R = Et, R1 = H, R2 = Me, R3 = Me, R4 = NH2, R5 = p-MeO)(Ie). A soln. of 0.05 mole Ie in 1000 ml. dry C5H5N and 6 g. Ac2O was kept 18 hrs. at room temp. to give I (R = Et, R1 = H, R2 = Me, R3 = Me, R4 = AcNH, R5 = p-MeO). Ie was treated with Me2SO4 and 10% NaOH at 0.degree. to 5.degree. to give I (R = Et, R1 = H, R2 = Me, R3 = Me, R4 = Me2N, R5 = p-MeO), which was hydrolyzed as above to the free acid. A cold mixt. of 5.4 ml. 25% aq. Me2NH, 3 ml. AcOH, and 2.25 ml. 40% aq. HCHO was added to 4.4 g. 2-ethyl-5-methylindole (IX), kept 5 hrs. at room temp., and treated with 25 ml. 10% KOH to give 2-ethyl-5-methylgramine (X), m. 100-3.degree.. A soln. of 2 g. X, 4 g. KCN, and 32 ml. 80% EtOH was refluxed 68 hrs. to give 1 g. III (R = H, R2 = Et, R3 = H, R4 = Me),m. 137-8.degree.. A slow stream of N was passed for 1 hr. through a stirred, refluxing (210.degree.) mixt. of 50 g. 2,4-dimethylpropionanilide, 50 g. Nah, and 500 ml. PhNEt2. H2O (250 ml.) was added to the hot soln. and the aq. phase worked up to give 38 g. IX, m. 72-84.degree.. A mixt. of 53.3 g. p-H2NC6H4SH (XI) in 200 ml. EtOH and 60.2 g. pClC6H4CHO (XlI) in 200 ml. EtOH was stirred 20 min. to give p-ClC6H4CH : NC6H4SH-p. This was added portionwise to a suspension of 11.52 g. NaH (52% in mineral oil) in 400 ml. HCONMe2 and treated with 35 g. MeI in 100 ml. HCONMe2 to give p-ClC6H4CH : NC6H4SMe-p (XIII). A suspension of 12 g. XIII in 300 ml. MeOH was reduced with 4 g. NaBH4 to give p-ClC6H4CH2NHC6H4SMe-p (XIV). A soln. of 60 g. XIV in 300 ml. AcOH was treated with 16 g. NaNO2 in 60 ml. H2O during 60 min. at 25-8.degree.. The resulting nitroso deriv. (3.8 g.) was reduced with Al amalgam (from 7 g. Al and 3 g. Hg(OAc)2 in iso-PrOH to

give N1 - p - chlorobenzyl - 4 - methylthiophenylhydrazine (XV).HCl, m. 140.5.degree.. XV (31 g.) was ring closed with 16 g. II in 400 ml. 7.5N ethanolic HCl to give 13 g. I (R = Et, R1 = H, R2 = Me, R3 = Me, R4 = MeS, R5 = p-Cl), which on hydrolysis gave the corresponding acid, m. 154-60.degree. (MeCN). A soln. of 120 g. PhSMe and 69 g. ClCH2OMe in 600 ml. AcOH was heated at 78-80.degree. for 2 days to give 68 g. p-MeSC6H4CH2Cl (XVI), b1 99.degree.. A cooled soln. (2.degree.) of 25 g. p-H2NC6H4CH2OH in 200 ml. H2O contg. 80 ml. concd. HCl was treated with a soln. of 15.5 g. NaNO2 in 40 ml. H2O, neutralized with AcOK, filtered, and the filtrate added to 97.6 g. K Et xanthate in 1000 ml. H2O at 75-80.degree.. The mixt. was heated on a steam bath 1 hr., the product (oil) isolated, and treated with 33 g. KOH in 300 ml. EtOH and 50.6 g. PhCH2Cl to give p-PhCH2SC6H4CH2OH (XVII), m. 75-81.degree.. A soln. of 10.7 g. XVII in 100 ml. SOCl2 at 0.degree. was kept 1 hr. to give p-PhCH2SC6H4CH2Cl, m. 91-3.degree.. A cooled suspension of 6 g. If (see below) in 150 ml. liquid NH3 was treated with 1.3 g. Na, to give I (R = H, R1 = H, R2 =Me, R3= Me, R4 = MeO, R5 = p-HS), m. 161-4.degree.. A soln. of 61 g. p-F3CC6H4Br in 60 ml. Et2O was added to a mixt. of 7.29 g. Mg shavings in 50 ml. dry Et2O. The mixt. was stirred and treated with 2 ml. freshly prepd. MeMgI in Et2O, 200 ml. Et2O, and refluxed 1.5 hrs. The soln. was cooled and treated with 81 g. HCONMePh and worked up to give p-F3CC6H4CHO (XVIII), b12 64.degree., n22D 1.4633. A soln. of 20.9 g. XVIII in 100 ml. MeOH was treated with 2.5 g. NaBH4 to give p-F3CC6H4CH2OH, b12 85-8.degree., which was converted to the acid chloride with SOCl2, b12 68.degree., n22D 1.4622. A soln. of 2 g. Ig (see below) and 25 ml. 30% NaOH in 150 ml. EtOH was refluxed 18 hrs. to give I (R = R1 = H, R2 = R3 = Me, R4 = MeO, R5 = CO2H), m. 230-4.degree.. A mixt. of 4.25 g. Id, 100 ml. Ac2O, and 100 ml. AcOH was reductively acetylated in the presence of 1 g. Pd-on-C to give I (R = Et, R1 = H, R2 = Me, R3 = Me, R4 = MeO, R5 = p-AcNH), which was hydrolyzed to the corresponding acid. A mixt. of 59.7 g. p-MeC6H4SO2NMe2 and 53.4 g. N-bromosuccinimide in 500 ml. CCl4 was refluxed 2.5 hrs. to give p-BrC6H4SO2NMe2, m. 85-108.degree.. A soln. of 36.02 g. MeP(Ph3)Br and 94.36 ml. of 1.10N BuLi in 500 ml. dry Et2O was stirred 1 hr. at room temp. under N, treated with 38 g. Et .alpha.-(1-p-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)-oxoacetate (XIX) in 260 ml. C6H6, then with 500 ml. Et2O, stirred 1 hr., heated 5 hrs. in a closed flask at 65-70.degree., and worked up to give Et .alpha.-(1-p-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)acrylate (XX), m. 94-5.degree.. XIX was hydrolyzed to the corresponding free acid, m. 187-8.degree.. A soln. of 19 g. (COCl)2 in 25 ml. Et2O was added rapidly to an ice cold mixt. of 35.7 g. 1-p-chlorobenzyl-2-methyl-5-methoxyindole in 900 ml. Et2O, stirred 2 hrs., and filtered. The filter cake was dissolved in 600 ml. EtOH, treated with 0.12 mole NaOEt, stirred 1 hr., and poured into an equal vol. H2O contg. 10ml. AcOH to give XIX, m. 113.degree.. To a soln. of 1.8 g. XX in 10 ml. tetrahydrofuran (THF) was added 4 g. CH2I2, 1.25 g. Zn-Cu couple, and 0.2 g. iodine in 20 ml. dry THF and stirred 20 hrs. under N to give 1.2 g. Et .alpha.-(1-p-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)cyclopropylcarboxylate, which was hydrolyzed to the corresponding acid, m. 220-4.degree.. p-MeOC6H4N:CHC6H3(OMe)2-2,4, m. 126-7.degree., obtained as above from 37 g. p-MeOC6H4NH2 and 50 g. 2,4-(MeO)2C6H3CHO in 250 ml. EtOH and in the presence of Raney Ni at 40 psi. of H was converted by treatment with NaNO2 and Al amalgam to N-(2,4-dimethoxybenzyl)-p-methoxyphenylhydrazine-HCl, m. 136-9.degree.. A hot soln. of racemic Ie (24.9 g.) and 9.5 g. (+)-.alpha.-PhCH2NH2 (XXI) in boiling EtOH was cooled to give pure (+)-.alpha.-Ie.(+)-.alpha.-XXI salt, m. 170-2.degree., [.alpha.]22D 38.5.degree. (c 1, MeOH). From the salt was regenerated in the usual manner pure (+)-.alpha.-Ie, m. 118.degree., [.alpha.]22D 62.4.degree. (c 0.94, EtOH). The following were obtained by similar resolutions: (+)-.alpha.-Ic.(+)-.alpha.-XXI, m. 148-9.degree., [.alpha.]22D 43 (c 1, MeOH); (+)-.alpha.-Ic, m. 156-7.degree., [.alpha.] 22D 60 (c 1, EtOH); and (-)-.alpha.-Ic, m. 153-4.degree., [.alpha.]23D -58.degree. (c 1, EtOH). A mixt. of 8.8 g. Ie and 14 g. urea was heated 1.5 hrs. at 190-200.degree.

to give the corresponding amide, m. 143-4.degree.. Ih (see below) was refluxed with Ac2O to give (1-p-chlorobenzyl-2-carboxy-5-methoxy-3-indolyl)acetic acid anhydride, m. 205-11.degree., which was treated with NaOEt in EtOH at 0.degree. to give I (R = Et, R1 = H, R2 = CO2H, R3 = H, R4 = MeO, R5 = p-Cl) (Ii), m. 214-16.degree.. A. soln. of 0.05 mole Ii in 200 ml. C6H6 was added dropwise to a soln. of 0.06 mole SOCl2 in 20 ml. C6H6 to give the corresponding 2-chlorocarbonyl deriv. (XXII). A soln. of 0.02 mole XXII in 100 ml. tetrahydrofuran was added dropwise to a soln. of Li tri-(tert-butoxy)aluminum hydride in tetrahydrofuran to give the corresponding 2-formyl deriv., which was reduced with NaBH4 to the 2-CH2OH compd. MeSH (24 g.) was bubbled into 350 ml. EtOH contg. 32.5 g. 86.5% KOH. This soln. was treated with 1.2 ml. H2O, then a soln. of 70.3 g. XII in 150 ml. EtOH, and refluxed 3 hrs. while MeSH was slowly bubbled in to give p-Me SC6H4CHO (XXIII). A mixt. of 20 g. XXIII, 8 g. Al[OCH(Me)2]3, and 300 ml. iso-PrOH was heated 3.5 hrs. and worked up to give p-MeSC6H4CH2OH (XXIV). A cooled soln. of 19.5 g. XXIV in 25 ml. C6H6 was treated with 23 g. SOCl2 to give XVI. Standard procedures are given for the prepn. of a number of metal salts of some of the above compds. The following I were similarly prepd. by the above procedures (R, R1, R2, R3, R4, R5, and m.p. given): Et, H, Me, Me, MeO, m-Cl, -; H, H, Me, Me, MeO, m-Cl, 191-2.degree.; Et, H, Me, Me, MeO, 2,4-Cl2, 130.degree.; H, H, Me, Me, MeO, 2,4-Cl2, 184-6.degree.; Et, H, Me, Me, Me, p-Cl, 89-90.degree.; H, H, Me, Me, Me, p-Cl, 185-6.degree.; Et, H, Me, Me, MeO, p-MeO, sirup; H, H, Me, Me, MeO, p-MeO, 153-3.5.degree.; Et, H, Me, Me, MeO, p-F, -; H, H, Me, Me, MeO, p-F, 164-5.degree.; Et, H, Me, Me, MeO, p-CHF2S, oil; H, H, Me, Me, MeO, p-CHF2S, 132-3.degree.; Et, H, Me, Me, MeO, p-CHF2O, oil; H, H, Me, Me, MeO, p-CHF2O, 144-6.degree.; Et, H, Me, Me, MeO, p-Cl, oil; H, H, Me, Me, MeO, p-Cl (Ic), 163-5.degree.; Me, Me, Me, H, MeO, p-Cl, -; H, Me, Me, H, MeO, pCl, -; Et, H, H, H, MeO, p-F, -; H, H, H, H, MeO, p-F, -; H, H, H, H, MeO, p-Cl, 144-8.degree.; Et, H, Me, Me, NO2, p-MeO (Id), -; H, H, Me, Me, NO2,.p-MeO, -; H, H, Me, Me, NH2, p-MeO, -; H, H, Me, Me, AcNH, p-MeO, -; H, H, Et, H, Me, p-Cl, -; Et, H, Me, Me, MeO, p-MeS, -; H, H, Me, Me, MeO, p-MeS, 170-1.degree.; H, H, Me, H, H, p-Cl, -; Et, H, Ph, H, MeO, p-Cl, -; H, H, Ph, H, MeO, p-Cl, -; H, H, Me, Me, MeO, p-MeS (Ie), 170-3.degree.; H, H, Me, Me, MeO, p-HS, -; H, H, Me, Me, MeO, p-PhCH2S (If), 150-3.degree.; Et, H, Me, Me, MeO, p-MeSO, -; H, H, Me, Me, MeO, p-MeSO, 98-101.degree. H, H, CF3, H, MeO, p-MeS, 168-72.degree.; Me, H, Me, H, MeO, p-MeS, -; H, H, Me, H, MeO, p-MeS, 155-6.5.degree.; Et, H, Me, H, MeO, p-MeS, 94-5.degree.; Et, H, Me, Me, Me, p-MeS, 111-13.degree.; H, H, Me, Me, Me, p-MeS, 184-7.degree.; H, H, Me, Me, MeO, pCF3, 176-80.degree.; Et, H, Me, Me, MeO, p-NC (Ig), 72.degree.; H, H, Me, Me, MeO, p-NC, 197-200.degree.; Et, H, Me, Me, MeO, p-NO2, 102-3.degree.; H, H, Me, Me, MeO, p-NO2, 188-90.degree.; Et, H, Me, Me, MeO, p-NMe2, -; H, H, Me, Me, MeO, p-NMe2, 193-4.degree.; Et, H, Me, Me, MeO, p-Me2NSO2, 140.degree.; H, H, Me, Me, MeO, pMe2NSO2, 156.5-8.5.degree.; Et, H, Me, Me, MeO, p-EtS, -; H, H, Me, Me, MeO, p-EtS, 126-33.degree.; Et, H, Me, Me, MeO, p-PhS, -; H, H, Me, Me, MeO, p-PhS, -; Et, H, H, H, MeO, pMeS, -; H, H, H, H, MeO, p-Cl, 146-8.degree.; H, H, CH2Ph, Me, MeO, p-Cl, -; H, H, CH2Ph, Me, MeO, p-Cl, -; Et, H, Me, Me, MeO, 2,4-(MeO)2, -; H, H, Me, Me, MeO, 2,4-MeO)2, -; Et, Me, Me, Me, MeO, p-MeS, -; H, Me, Me, Me, MeO, p-MeS, -; and H, H, CO2H, H, MeO, p-Cl (Ih), 213-18.degree.. The following III derivs. were similarly prepd. by the procedures given above (R, R2 R3, and R4 given); Et, Me, Me, Me, b1 150-70.degree., m. 88-8.5.degree.; Et, H, H, MeO; and Et, Me, H, Cl, m. 85.degree.. Also prepd. by the procedure given above was p-O2NC6H4CH2N(NH.HCl)C6H4MeO-p, m. 147-50.degree..

L8 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1965:488799 HCAPLUS
DN 63:88799
OREF 63:**16308a-h,16309a-c**
TI Indolyl aliphatic acids
IN Sarett, Lewis H.; Shen, Tsung Y.

PA Merck & Co., Inc.
SO 23 pp.
DT Patent
LA Unavailable
NCL 260319000
CC 37 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3196162		19650720	US	19590903

GI For diagram(s), see printed CA Issue.

AB The title compds. (Ia) are antiinflammatory and sunscreening agents, some of which have antipyretic action p-Methoxyphenyl-hydrazine-HCl (25 g.) and 20 g. Et .alpha.-methyllevulinate in 250 ml. 2N ethanolic HCl was refluxed to give Et .alpha.-(2-methyl-5-methoxy-3-indolyl)propionate (I), b0.25 150-3.degree. m. 53-5.5.degree.. Et .alpha.-(2,5-dimethyl-3-indolyl)propionate, b1 150-170.degree. (bath temp.), m. 88-8.5.degree. (petroleum ether), was similarly prepd. I was hydrolyzed to the free acid, m. 163-5.degree. (aq. EtOH). I (13 g.) in 75 ml. dimethylformamide (II) was added to a stirred suspension of 2.5 g. of a NaH-mineral oil dispersion (contg. 52 wt.-% NaH) in 100 ml. II. The mixt. was stirred at room temp. for 1 hr., then 8 g. o-chlorobenzyl chloride was added slowly. The resulting mixt. kept at room temp. 14 hrs. gave Et .alpha.-(1-o-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)propionate (III), 118-122.degree.. III was sapond. to give the free acid, m. 191-2.degree. (benzene). In a similar manner, the following Ia (R1 = R6 = H, R2 = R3 = Me), were prepd. (R, R4, R5, and m.p. given): H, OCH3, m-Cl, 191-2.degree.; Et OCH3, o,p-di-Cl, 130.degree.; H, OCH3, o,p-di-Cl 184-6.degree.; Et CH3, p-Cl, 89-90.degree.; H, CH3, p-Cl, 185-6.degree.; H, OCH3, p-OCH3, 153-3.5.degree.; H, OCH3, p-F, 164-5.degree.; Et, OCH3, p-SCHF2, -; H, OCH3, p-SCHF2, 132-3.degree.; Et, OCH3, p-OCHF2, -; H, OCH3, p-OCHF2, 144-6.degree.; H, OCH3, p-Cl, 163-5.degree.; H, OCH3, p-SCH3, 170-1.degree.; H, OCH3, p-SCH2Ph, 150-3.degree.; H, OCH3, p-SH, 161-4.degree.; H, OCH3, p-SOCH3, 194-6.degree.; H, OCH3, p-SOCH3, 98-101.degree.; Et, CH3, p-SCH3, 111-13.degree.; H, CH3, p-SCH3, 184-7.degree.; H, OCH3, p-CF3, 176-80.degree.; Et, OCH3, p-CN, 72.degree.; H, OCH3, p-CN, 197-200.degree.; H, OCH3, p-COOH, 230-4.degree.; Et, OCH3, p-NO2, 102-3.degree.; H, OCH3, p-NO2, 188-90.degree.; H, OCH3, p-N(CH3)2, 193-4.degree.; Et, OCH3, p-SO2N- (CH3)2, 140.degree.; H, OCH3, p-SO2N(CH3)2, 156.5-8.5.degree.; H, OCH3, p-SEt, 126-33.degree.. .alpha.-(1-p-Methylthiobenzyl-2-methyl-5-methoxy-3-indolyl)propionic acid (IV) (8.8 g.) and 14 g. urea was heated at 190-200.degree. for 1.5 hrs. to give the amide of IV m. 143-4.degree.. IV (4.45 g.) was slurried in 12 ml. MeOH, 5.2 ml. 2.21N NaOCH3 in MeOH was added under N and the soln. was concd. to a sirup to give the Na salt of IV. The Al salt of IV was also prepd. In the prepn. of .alpha.-(1-p-chlorobenzyl-2-methyl-5-methylthio-3-indolyl)propionic acid (V), N-p-chlorobenzylidene-4-mercaptoaniline (VI) was prepd. from 53.3 g. p-aminothiophenol in 200 ml. EtOH and 60.2 g. p-chlorobenzaldehyde in 200 ml. EtOH. VI (58.2 g.) was treated with 11.52 g. NaH (52% in mineral oil) in 400 ml. II and 35 g. CH3I in 100 ml. II to give N-p-chlorobenzylidene-4-methylthioaniline (VII). VII was treated with NaBH4 to give N-p-chlorobenzyl-4-methylthioaniline. The corresponding nitroso deriv. was prepd. and reduced to give N'-p-chlorobenzyl-4-methylthiophenylhydrazine-HCl m. 140.5.degree. (EtOH). Ring closure of the hydrazine with Et .alpha.-methyllevulinate gave the Et ester of V as a yellow sirup. The ester was sapond. to V, m. 154-60.degree. (acetonitrile). The following intermediates were also prepd.: p-difluoromethylthiotoluene, b0.35 32-4.degree., n23D 1.5092; p-difluoromethylthiobenzyl bromide, b0.3 74.degree., n22D 1.5622; p-difluoromethoxytoluene, b. 165-7.degree.; p-difluoromethoxybenzyl bromide, b0.2 50-2.degree. n23D 1.5170; p-methylthiobenzyl chloride b1 99.degree.; p-trifluoromethylbenzaldehyde, b12 64.degree., n22D 1.4633; p-trifluoromethylbenzyl chloride, b12 68.degree., n22D 1.4622;

p-trifluoromethylbenzyl alcohol, b12 85-8.degree., n22D 1.4562; N'-(p-nitrobenzyl)-N-(p-methoxyphenyl)hydrazine-HCl, 147-150.degree.; NN-dimethyl-p-bromomethylbenzenesulfonamide, 85-108.degree.; p-ethylthiobenzyl chloride, b. 92-103.degree./250-400 m.mu.; phenylthiobenzyl chloride (39%, by analysis), b. 85-145.degree./50 m.mu.; N-(o,p-dimethoxybenzyl)-p-methoxyaniline, 126-7.degree.; N'(o,p-dimethoxybenzyl)-N-(p-methoxyphenyl)hydrazine-HCl, 136-9.degree.. Also prepd. were the following Ia (R3 = R6 = H) (R, R1 , R2 , R4 , R5, and m.p. given): H, H, H, OCH3, p-Cl, 144-8.degree.; H, H, CF3, OCH3, p-SCH3, 168-72.degree.; H, H, CH3, OCH3 , p-SCH3, 155-6.5.degree.; Et, H, CH3, OCH3, p-SCH3, 94-5.degree.; H, H, H, OCH3, p-Cl, 146-8.degree.; H, H, COOH, OCH3, p-Cl, 213-18.degree.; Et, H, COOH, OCH3, p-Cl, 214-16.degree.; H, H, H, OCH3, p-Cl, 146-8.degree.. The following intermediates were prepd.: 2-ethyl-5-methylindole, 72-4.degree.; 2-ethyl-5-gramine, m. 100-3.degree.; .alpha.-(2-ethyl-5-methyl-3-indolyl)acetic acid, m. 137-8.degree.; Et 2-methyl-5-chloro-3-indolylacetate, m. 85.degree.. Oxalyl chloride (19 g.) in 25 ml. ether was added rapidly to an ice cold mixt. of 35.7 g. 1-p-chlorobenzyl-2-methyl-5-methoxyindole in 900 ml. ether and the mixt. stirred for 2 hrs.; the solid recovered was added to 660 ml. EtOH and treated with 0.12 moles NaCl. After being stirred 1 hr., the mixt. was poured into an equal vol. of H2 O contg. 10 ml. acetic acid to give Et .alpha.-(1-p-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)oxoacetate (VIII), m. 113.degree.. VIII (38 g.) in 260 ml. benzene and 500 ml. dry ether was added to a mixt. of 500 ml. dry ether, 36.02 g. triphenylphosphonium bromide, and 94.36 ml. 1.10N BuLi under N. After stirring 1 hr., the mixt. was heated in a closed flask at 65-70.degree. for 5 hrs. to give Et .alpha.-(1-p-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)acrylate (IX), m. 94-5.degree.. The free acid m. 187-8.degree. (EtOH). IX (1.8 g.) in 10 ml. dry tetrahydrofuran was added to 4 g. diiodomethane, 1.25 g. Zn-Cu couple, and 0.2 g. iodine in 20 ml. dry tetrahydrofuran. The mixt. was refluxed to give Et .alpha.-(1-p-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)cyclopropa-necarboxylate (X). X was hydrolyzed to the free acid, m. 220-4.degree.. In addition, racemic and optically active forms were prepd.: (+)-.alpha.-(1-p-methylthiobenzyl-2-methyl-5-methoxy-3-indolyl)pr-opionic acid (+)-.alpha.-phenethylamine salt m. 170-2.degree., [.alpha.]22 D 38.5.degree. (c 1, MeOH); the free acid of the preceding salt, m. 118.degree., [.alpha.]22 D 62.4.degree. (c 0.94, EtOH); (+)-.alpha.-(1-p-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)propionic acid (+)-.alpha.-phenethylamine salt, m. 148-9.degree., [.alpha.]22 D 43.degree. (c 1, MeOH); the free acid (XI) of the preceding salt m. 156-7.degree., [.alpha.]22 D 60.degree. (c 1, EtOH); the dl form of XI; the (-) form of XI, m. 153-4.degree., [.alpha.]23D -58.degree. (c 1, EtOH); (-)-.alpha.-(1-p-chlorobenzyl-2-methyl-5-methoxy-3-indolyl)propionic acid (-)-.alpha.-phenethylamine salt. Racemic forms of .alpha.-[1-p-fluoro(and methoxy)benzyl-2-methyl-5-methoxy-3-indolyl]propionic acids and of 1-(1-p-methylthio-benzyl-2,5-dimethyl-3-indolyl)propionic acid were also prepd.

L8 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1965:462954 HCAPLUS
DN 63:62954
OREF 63:**11509b-f**
TI 1-Aryloxindoles
IN Archer, Sydney; Schulenberg, John W.
PA Sterling Drug Inc.
SO 10 pp.
DT Patent
LA Unavailable
NCL 260139000
CC 37 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI US 3189617 19650615 US 19610203
GI For diagram(s), see printed CA Issue.
AB A mixt. of I and II was obtained on heating III with a strong base under anhyd. conditions. The 3-aroyl group in I can be split off to give a 1-aryloxindole (IV). I and IV possess hypotensive activity, while II have antibacterial properties. On mixing 56.5 g. Me 2-benzamidophenylacetate and 43.7 g. PCl5, a spontaneous reaction occurred, after which the mixt. was heated on a steam bath until HCl evolution ceased and the POCl3 removed in vacuo at 50.degree. to yield PhCCl:NA (V) (A = 2-MeO2CC6H4 throughout), a red oil. A soln. of 35 g. Me salicylate in 50 ml. MeOH was added quickly to a stirred soln. of 12.4 g. MeONa in 200 ml. MeOH under N, then a soln. of V in 65 ml. abs. Et2O added during 5 min., and the mixt. stirred 3 hrs. at room temp. to give 59.2 g. AN:CPh(OC6H4CO2Me-2) (VI), m. 62.2-5.2.degree. (MeOH). VI (39.2 g.) was heated 12 min. at 280-95.degree. to yield 32.6 g. III (Z = Me, Ar = Ph, Ar1 = A) (VII), m. 117-21.8.degree. (MeOH). To a stirred mixt. of 19 g. VII in 125 ml. hot C6H6 in a N atm. was added 2.7 g. MeONa, the mixt. refluxed 1 hr. while distd. and adding C6H6, then cooled, and poured on dil. HCl, whereupon a mixt. of two compds. sepd., from which was obtained 12.6 g. I CAr = Ph, Ar1 = A) (VIII), m. 135.2-8.0.degree. (free acid m. 208.610.0.degree.), and II (Z = H, Ar = Ph, Ar1 = A), m. 254-60.degree. (MeOH). A soln. of 6.8 g. VIII, 60 ml. AcOH, and 60 ml. 48% HBr was refluxed 1 hr. to yield 1.9 g. 1-(2-carboxyphenyl)oxindole (IX), m. 207.5-9.5.degree.. A soln. of 16.1 g. VII, 35 g. KOH, 150 ml. H2O and 75 ml. dioxane was refluxed 16 hrs. to give o-(2-carboxyanilino)phenylacetic acid, m. 187.0-90.6.degree., which refluxed with 48% HBr and AcOH yielded IX. Similarly prepd. were 2-EtO2CCH2C6H4N: CPh(OC6H4CO2Me-2), m. 92.5-90.degree.; III (Z = Et, Ar = Ph, Ar1 = A), m. 114.5-16.degree.; mixt. of I(Ar = Ph, Ar1 = EtO2CC6H4) (X), m. 142-4.degree. and II (Z = H, Ar = Ph, Ar1 = 2-EtO2CC6H4), m. 278-81.degree.. A mixt. of 4.9 g. X, 40 ml. EtOH, 30 ml. concd. HCl and 20 ml. dioxane was refluxed 12 hrs. to give 1-(2-carbethoxy)oxindole, m. 118.5-21.5.degree.. Also prepd. were III (Z = Me, Ar = Ar1 = Ph), m. 132.5-4.5.degree.; mixt. of I (At = Ar1 = Ph) (XI), m. 116.6-19.4.degree. and II (Z = Me, Ar = Ar1 = Ph) (XII), m. 193.5-5.0.degree.. XI was also obtained by condensing 1-phenyloxindole with PhCO2Et in the presence of EtONa. Ph2NN:(Ph)CH2CO2Et on heating with EtOH and HCl yielded II (Z = Et, Ar = Ar1 = Ph), m. 149-50.5.degree. [free acid m. 247.6.degree. (decompn.); Na-salt m. >300.degree.], whose Me ester was identical with XII. Pertinent uv and ir spectral data are given for most of these compds.

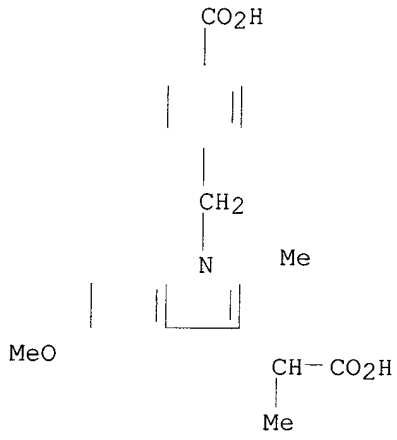
L8 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1961:137418 HCAPLUS
DN 55:137418
OREF 55:**25908i,25909a-i,25910a**
TI An unusual base-catalyzed cyclization
AU Schulenburg, John W.; Archer, S.
CS Sterling-Winthrop Research Inst., Rensselaer, NY
SO J. Am. Chem. Soc. (1961), 83, 3091-6
DT Journal
LA Unavailable
CC 10G (Organic Chemistry: Heterocyclic Compounds)
AB The reaction of o-MeO2CCH2C6H4NBzC6H4CO2Me-o (I) with NaOMe gave 3-benzoyl-1-(o-carbomethoxyphenyl)oxindole (II) and a related indole, probably 1-(o-carbomethoxyphenyl)-2-phenyl-3-indolecarboxylic acid (III), instead of the expected Dieckmann product. o-BzPhNC6H4CH2CO2Me (IV) yielded similarly 3-benzoyl-1-phenyloxindole (V) and Me 1,2-diphenyl-3-indolecarboxylate (VI). o-O2NC6H4CH2CO2Me (VII) in MeOH hydrogenated over Pt, and the resulting crude o-H2N analog (VIII) of VII, orange oil, treated with BzCl in C5H5N gave 72-8% N-Bz deriv. (IX) of VIII. o-O2NC6H4CH2CO2Et hydrogenated in EtOH and treated with BzCl-C5H5N gave o-BzNHC6H4CH2CO2Et (X). IX (56.5 g.) and 43.7 g. PCl5 heated on the steam bath and evapd. in vacuo at 50.degree. and the residue codistd. with

PhMe left red oily o-PhCCl:NC6H4CH2CO2Me (XI). o-HOC6H4CO2Me (XII) (35.0 g.) in 50 cc. MeOH added with stirring to 12.4 g. NaOMe in 200 cc. MeOH under N, treated with the XI in 65 cc. dry Et2O during 5 min., stirred 3 hrs. at room temp., dild. with H2O, and extd. with Et2O yielded 59.2 g. o-MeO2CCH2C6H4N: CPhOC6H4CO2Me-o (XIII), m. 62-5.degree. (MeOH). XI (from 51 g. X and 37.5 g. PCl5) in 50 cc. dry Et2O added to 10.8 g. NaOMe in 200 cc. MeOH and 30.4 g. XII in 50 cc. MeOH gave 47.2 g. o-EtO2CCH2C6H4N:CPhOC6H4CO2Me-o (XIV), m. 92.5-96.degree. (abs. EtOH). XIII (39.2 g.) heated 12 min. at 280-95.degree. gave 32.6 g. I, m. 115-18.5.degree. (MeOH). XIV (27.2 g.) pyrolyzed during 12 min. yielded 24.8 g. o-EtO2CCH2C6H4NBzC6H4CO2Me-o (XV), m. 114.5-16.degree.. I (19.0 g.) in 125 cc. hot C6H6 treated with stirring under N with 2.7 g. NaOMe, refluxed 1 hr. with removal of solvent while the vol. was maintained above 50 cc. by the occasional addn. of dry C6H6, cooled, and worked up gave 12.6 g. II, m. 136-8.degree. (MeOH); it gave a dark green color with FeCl3. A similar run performed in PhMe, and the crude product boiled with cyclohexane left a small amt. of III, m. 254-60.degree. (MeOH); the filtrate gave II. XV (43.0 g.) in 125 cc. dry PhMe refluxed 2 hrs. with dry NaOEt (from 2.76 g. Na) under N gave 29.0 g. Et ester analog (XVI) of II, m. 142-4.degree. (EtOAc); it gave a dark green color with FeCl3; the mother liquor yielded 2 g. Et ester analog of III, m. 278-81.degree. (EtOH). Crude XVI, m. 128-33.degree., was also obtained from I and NaOEt in PhMe. I (16.1 g.), 35 g. KOH, 150 cc. H2O, and 75 cc. dioxane refluxed 16 hrs., washed with Et2O, and acidified below 15.degree. with excess HCl, and the gummy ppt. extd. with Et2O gave 3.0 g. o-HO2CCH2C6H4NHC6H4CO2H-o (XVII), m. 181-3.degree. (decompn.) (EtOAc). XVI (2 g.) refluxed 2 hrs. with 3 g. KOH in 60 cc. H2O yielded 550 mg. XVII, m. 181-3.degree. (decompn.) (EtOAc). I (2 g.) refluxed 1 hr. with 3 g. KOH in 50 cc. H2O and acidified gave o-[o-HO2CC6H4NBz]C6H4CH2CO2Me, m. 208-10.degree. (Me2CO-hexane). XVII (0.8 g.), 10 cc. AcOH, and 10 cc. 48% HBr refluxed 0.5 hr. gave 1-(o-carboxyphenyl)oxindole (XVIII), m. 206-9.degree. (EtOAc). II (6.8 g.), 60 cc. AcOH, and 60 cc. 48% HBr refluxed 1 hr. gave 1.9 g. XVIII, m. 207.5-9.5.degree. (EtOAc-hexane); XVIII was also obtained similarly from XVI. XVI (4.9 g.), 40 cc. EtOH, 30 cc. concd. HCl, and 20 cc. dioxane refluxed 12 hrs. yielded 1.2 g. Et ester of XVIII, m. 118.5-21.5.degree. (iso-PrOH). II (10.0 g.), 20 g. K2CO3, 500 cc. MeOH, and 125 cc. H2O refluxed 3 hrs. gave 6.3 g. light yellow 3-Bz deriv. of XVIII, m. 206-9.degree. (C6H6); it gave a green color with FeCl3. IV (1.38 g.) cyclized in the usual manner with 270 mg. NaOMe, dild. with H2O, extd. with CHCl3, and acidified with HCl yielded 420 mg. V, m. 118-21.degree. (iso-PrOH); it gave an intense color with FeCl3; the CHCl3 ext. evapd. gave 90 mg. VI, needles, m. 193.5-95.degree. (MeOH). 1-Phenyloxindole (8.4 g.), 50 cc. EtOH, and 15 g. BzOEt refluxed 2 hrs. with NaOEt in 40 cc. abs. EtOH (from 2.3 g. Na) gave 2.3 g. V, m. 117.5-20.5.degree. (isoPrOH), and some unreacted 1-phenyloxindole. BzCH2-CO2Et and Ph2NNH2 gave PhC(:NNPh2)CH2CO2Et; a 39-g. portion in 250 cc. warm EtOH treated with 250 cc. EtOH satd. with dry HCl and refluxed 1 hr. yielded 17.5 g. Et ester (XIX) of 1,2-diphenyl-3-indolecarboxylic acid (XX), m. 149-50.5.degree. (EtOH). XIX (3 g.), 25 cc. 35% aq. NaOH, 15 cc. H2O, and 50 cc. MeOH refluxed 18 hrs., cooled, and filtered, and the residual Na salt dissolved in hot H2O and treated with excess HCl gave XX, m. 244-5.degree. (decompn.) (Me2CO); Na salt, needles, m. above 300.degree. (H2O). XX (1 g.) and 10 cc. SOCl2 refluxed 45 min. and evapd. in vacuo, and the residue refluxed 45 min. with 10 cc. MeOH yielded VI, needles, m. 195-6.degree. (MeOH). V (1 g.), 1 g. NaOMe, and 15 cc. dry xylene refluxed 5 hrs. gave only a trace of neutral material; the acid fraction gave unchanged V. V (0.8 g.) and 20 cc. alc. HCl refluxed 3 hrs. gave 1-phenyloxindole, m. 121-3.degree. (95% EtOH). V (0.5 g.), 30 cc. EtOH, 10 cc. concd. aq. HCl, and 10 cc. H2O refluxed 5 hrs. gave only 1-phenyloxindole.

L8 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS
AN 1961:27828 HCAPLUS

DN 55:27828
OREF 55:**5461c-i,5462a**
TI Syntheses and spectroscopic properties in the ultraviolet region of .alpha.-substituted .alpha.-chloroselenophene derivatives
AU Chierici, Luigi; Pappalardo, Giovanni
CS Univ. Parma, Italy
SO Gazz. chim. ital (1959), 89, 1900-9
DT Journal
LA Unavailable
CC 10G (Organic Chemistry: Heterocyclic Compounds)
AB cf. CA 53, 18000d. POCl3 (9.4 g.) and 8.1 g. PhNMeCHO in 20 ml. PhCl stirred 30 min. at 50.degree. with addn. of 12.3 g. 2-ClC4H3Se (I), the mixt. stirred 18 hrs. at 20.degree., poured into cracked ice, extd. with Et2O, the ext. neutralized with NaHCO3, dried (Na2SO4), evapd., and the residue distd. gave faintly yellow oily 2-ClC4H2SeR-5 (II, R = CHO) (III), b15 109.degree. phenylhydrazone m. 131.degree.; semicarbazone m. 209.degree. (alc.). I (16.4 g.) and 1.17 g. 83% H3PO4 stirred 3 hrs. in 11.9 g. Ac2O at 130.degree., kept 12 hrs. at 20.degree., poured into 200 ml. H2O, the neutralized (NaHCO3) soln. extd. repeatedly with Et2O, the dried (CaCl2) ext. evapd., and the residue crystd. (dil. alc.) gave II (R = Ac) (IV), m. 57-8.degree.; phenylhydrazone m. 128.degree. (alc.); semicarbazone m. 228.degree. (dil. alc.). NaOH (4 g.) in 6 ml. H2O and 25 g. ice satd. with 2.8 g. Cl and stirred at 70.degree., 1.7 g. finely powd. I slowly added at 40.degree., the mixt. treated at 0.degree. with 1.4 g. NaHSO3 in concd. aq. soln., acidified with HCl, filtered, and the product (90%) crystd. from dil. alc. gave II (R = CO2H) (V), m. 172.degree.. AgNO3 (3.75 g.) and 1.75 g. NaOH in 15 ml. H2O at 0.degree. (ice bath) stirred with dropwise addn. of 2 g. III, the mixt. stirred 30 min., filtered, the ppt. washed with ice H2O, the filtrate and washings acidified with dil. HCl, and the ppt. (60%) crystd. from dil. alc. gave V, also produced in 19% yield by treating 2 g. 2-C4H3SeCO2H in 120 ml. AcOH at 20.degree. with 1 g. Cl, keeping the mixt. several min. before pouring into 700 ml. ice H2O, and keeping the mixt. 12 hrs. at room temp. V (2.5 g.) in 50 ml. MeOH satd. with dry HCl, the mixt. heated 20 min. on a steam bath, concd. to 20 ml., poured into 200 ml. H2O, neutralized with NaHCO3, and extd. with Et2O gave II (R = CO2Me) (VI), m. 27-8.degree. (dil. alc.). Similarly was produced the corresponding II (R = CO2Et) (VII), b14 120.degree.. V (3 g.) treated at 30.degree. with 5.7 ml. SOCl2 with evolution of HCl, the mixt. heated 20 min. at 35.degree., cooled with ice, dild. with 50 ml. Et2O, satd. with dry NH3, the product washed repeatedly with H2O, extd. with Et2O, and the dried (CaCl2) ext. evapd. gave II (R = CONH2) (VIII), m. 117.degree. (abs. alc.). Similarly were obtained II (R = CONHMe) (IX), m. 163.degree. (abs. alc.), and II (R = CONMe2) (X), b14 110.degree.. The ultraviolet absorption curves of II were scarcely affected by the solvent (95% alc. or C6H14) and the max. were tabulated [compd., .lambda. in m.mu. (log .epsilon.) in C6H14 and 95% alc. given]: I, 244.5, - (4.00, -), 245.5, - (4.00, -); III, 300 and 279 (3.90, 4.04), 307 and 281 (3.88, 4.04); IV, 301 and 279 (3.91, 4.06), 306 and 282 (3.90, 4.05); V, 290 and 275 (4.03, 4.08), 270 (4.05); VI, 285 and 272 (4.01, 4.08), 287 and 273 (4.00, 4.08); VII, 286 and 271 (4.04, 4.12), 287 and 273 (3.99, 4.10); VIII, - (-), 287 and 273 (3.94, 4.02); IX, - (-), 286 and 276 (3.99, 4.05); X, 307 and 284 (3.94, 4.07), 286 and 272 (4.02, 4.09). The 2 original bands of C4H4Se at 232 and 251 m.mu. were fused by the introduction of .alpha.-Cl to give a single band at 244.5 m.mu. (log .epsilon. 4.00), analogous to that of the corresponding .alpha.-BrC4H3Se, .lambda. 250 m.mu. (log .epsilon. 3.92). Similarly, the 2 bands of .alpha.-RC4H2Se located in the region 260-300 m.mu. were similarly compressed by introduction of the .alpha.'-Cl atom. The variation in energy due to the substitution of Cl was of the same order as that induced by Br in the corresponding Br derivs. In comparison with the isosteric thiophenes, the results showed that the aromatic character of the selenophene nucleus could be considered equal to or a little superior to that of the thiophene nucleus.

96761-91-0 97152-77-7 97257-35-7 101316-92-1 101698-87-7 101918-24-5
102130-47-2 102263-44-5 102602-92-6 106249-10-9 106524-27-0
IT **3447-34-5**
RN 3447-34-5 HCAOLD
CN Indole-3-acetic acid, 1-(p-carboxybenzyl)-5-methoxy-.alpha.,2-dimethyl-
(7CI, 8CI) (CA INDEX NAME)



L6 ANSWER 2 OF 7 HCAOLD COPYRIGHT 2002 ACS
AN CA65:3840e CAOLD
TI .alpha.-(1-benzyl-3-indolyl)alkanecarboxylic acids
AU Sarett, Lewis H.; Shen, T. Y.
PA Merck & Co., Inc.
DT Patent

PATENT NO.	KIND	DATE
US 3242193		1966

IT 349-95-1 455-19-6 874-87-3 939-99-1 1129-01-7 1140-46-1
1140-47-2 1208-87-3 1568-47-4 1583-83-1 1703-96-4 1959-23-5
1995-51-3 3446-61-5 3446-65-9 3446-67-1 3446-68-2 3446-69-3
3446-75-1 3446-77-3 3446-79-5 3446-80-8 3446-81-9 3446-82-0
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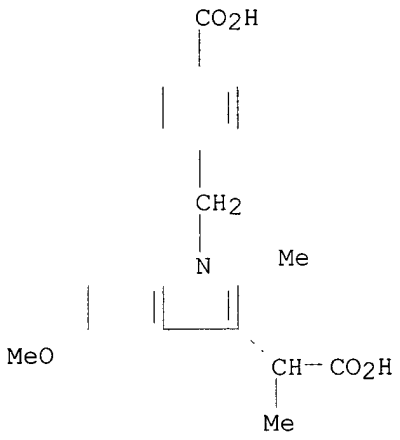
6644-59-3 6644-65-1 6715-60-2 6768-99-6 6769-00-2 6769-01-3
6827-79-8 95291-44-4 97254-55-2 97254-56-3 102602-92-6 106524-27-0
IT **3447-34-5**
RN 3447-34-5 HCAOLD
CN Indole-3-acetic acid, 1-(p-carboxybenzyl)-5-methoxy-.alpha.,2-dimethyl-
(7CI, 8CI) (CA INDEX NAME)



L6 ANSWER 3 OF 7 HCAOLD COPYRIGHT 2002 ACS
AN CA65:688d CAOLD
TI indolyl aliphatic acids
AU Sarett, Lewis H.; Shen, T. Y.
PA Merck & Co., Inc.
DT Patent

PATENT NO.	KIND	DATE
US 3242162		1966

IT 349-95-1 455-19-6 622-38-8 874-87-3 939-99-1 1129-01-7
1140-46-1 1140-47-2 1208-87-3 1568-47-4 1583-83-1 1959-23-5
3446-65-9 3446-67-1 3446-68-2 3446-69-3 3446-75-1 3446-77-3
3446-79-5 3446-80-8 3446-81-9 3446-82-0 3446-83-1 3446-91-1
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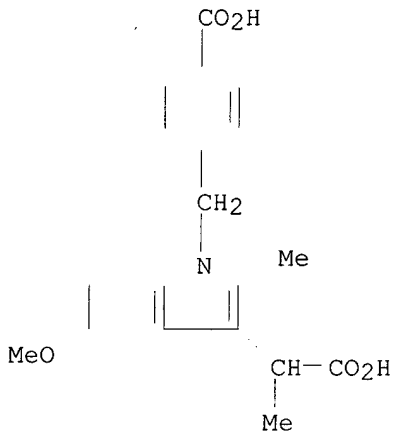
3449-17-0 3449-19-2 3526-18-9 3526-20-3 3526-23-6 3526-24-7
3721-30-0 3721-31-1 3721-33-3 3721-34-4 3875-69-2 4556-90-5
4648-25-3 6211-92-3 6260-37-3 6260-39-5 6260-41-9 6260-66-8
6260-95-3 6514-35-8 6514-89-2 6825-11-2 95291-44-4 102603-08-7
106524-27-0

IT **3447-34-5**
RN 3447-34-5 HCAOLD
CN Indole-3-acetic acid, 1-(p-carboxybenzyl)-5-methoxy-.alpha.,2-dimethyl-
(7CI, 8CI) (CA INDEX NAME)



L6 ANSWER 4 OF 7 HCAOLD COPYRIGHT 2002 ACS
AN CA63:16308a CAOLD
TI indolyl aliphatic acids
AU Sarett, Lewis H.; Shen, T. Y.
PA Merck & Co., Inc.
DT Patent

PATENT NO.	KIND	DATE
US 3196162		1965

IT 349-95-1 455-19-6 622-38-8 874-87-3 939-99-1 1129-01-7
1140-46-1 1140-47-2 1208-87-3 1568-47-4 1583-83-1 1703-96-4
1959-23-5 1995-51-3 3446-67-1 3446-68-2 3446-69-3 3446-72-8
3446-75-1 3446-77-3 3446-78-4 3446-79-5 3446-80-8 3446-81-9
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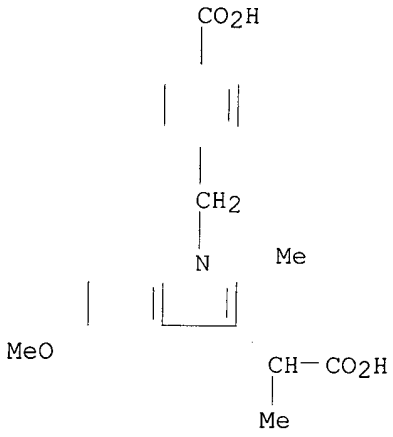
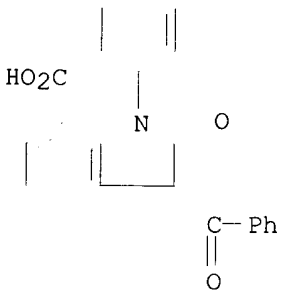
IT **3447-34-5**
RN 3447-34-5 HCAOLD
CN Indole-3-acetic acid, 1-(p-carboxybenzyl)-5-methoxy-.alpha.,2-dimethyl-(7CI, 8CI) (CA INDEX NAME)



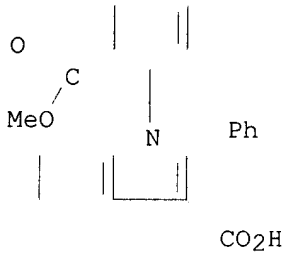
L6 ANSWER 5 OF 7 HCAOLD COPYRIGHT 2002 ACS
AN CA63:11509b CAOLD
TI 1-aryloxindoles
AU Archer, Sydney; Schulenberg, J. W.
PA Sterling Drug Inc.
DT Patent

PATENT NO.	KIND	DATE
US 3189617		1965

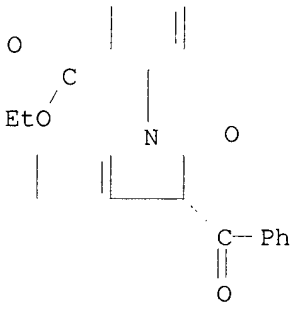
IT 3188-63-4 3192-49-2 **3283-76-9** **3283-77-0**
3283-78-1 3283-83-8 3283-84-9 **3283-85-0** 3283-86-1
3283-87-2 3283-88-3 3409-01-6 3409-27-6 3471-95-2
3547-22-6 **3549-84-6** 3549-85-7 3559-26-0
4548-68-9 5144-01-4 92874-56-1
IT **3283-76-9** **3283-77-0** **3283-85-0**
3547-22-6 **3549-84-6**
RN 3283-76-9 HCAOLD
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)- (6CI, 7CI, 8CI) (CA INDEX NAME)



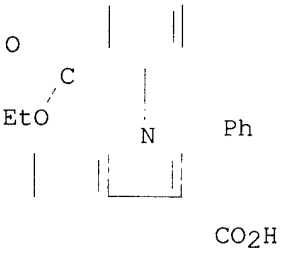
RN 3283-77-0 HCAOLD
CN Indole-3-carboxylic acid, 1-(o-carboxyphenyl)-2-phenyl-, 1-methyl ester (7CI, 8CI) (CA INDEX NAME)



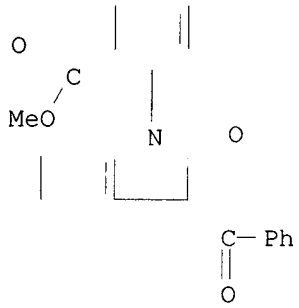
RN 3283-85-0 HCAOLD
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)-, ethyl ester (6CI, 7CI, 8CI) (CA INDEX NAME)



RN 3547-22-6 HCAOLD
CN Indole-3-carboxylic acid, 1-(o-carboxyphenyl)-2-phenyl-, 1-ethyl ester (7CI, 8CI) (CA INDEX NAME)



RN 3549-84-6 HCAOLD
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)-, methyl ester (6CI, 7CI, 8CI) (CA INDEX NAME)



L6 ANSWER 6 OF 7 HCAOLD COPYRIGHT 2002 ACS
AN CA55:25908i CAOLD
TI unusual base-catalyzed cyclization
AU Schulenberg, John W.; Archer, S.
IT 832-00-8 **3283-76-9** **3283-77-0** 3283-78-1
3283-83-8 3283-84-9 **3283-85-0** 3283-86-1 3283-87-2
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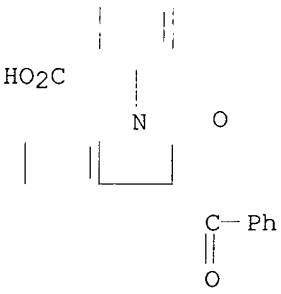
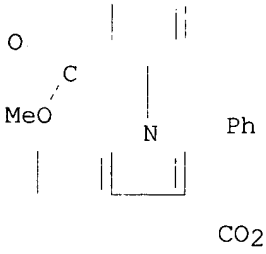
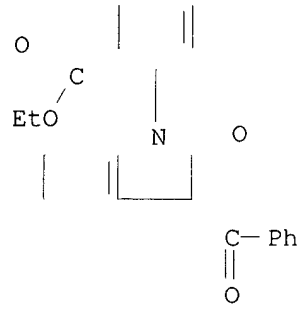
3547-22-6 **3549-84-6** 3549-85-7 3559-26-0
3812-14-4 4548-68-9 5144-01-4 35613-44-6 64959-58-6 90920-86-8
99172-83-5 101877-87-6 114795-01-6
IT **3283-76-9** **3283-77-0** **3283-85-0**
3547-22-6 **3549-84-6**
RN 3283-76-9 HCAOLD
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)- (6CI, 7CI, 8CI) (CA INDEX NAME)



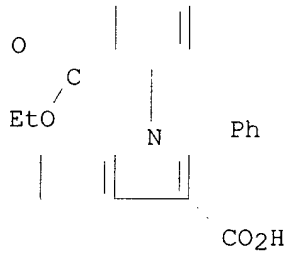
RN 3283-77-0 HCAOLD
CN Indole-3-carboxylic acid, 1-(o-carboxyphenyl)-2-phenyl-, 1-methyl ester (7CI, 8CI) (CA INDEX NAME)



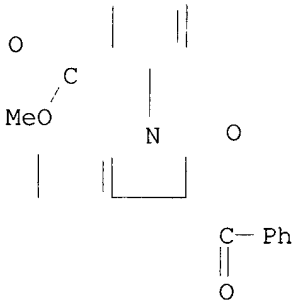
RN 3283-85-0 HCAOLD
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)-, ethyl ester (6CI, 7CI, 8CI) (CA INDEX NAME)



RN 3547-22-6 HCAOLD
CN Indole-3-carboxylic acid, 1-(o-carboxyphenyl)-2-phenyl-, 1-ethyl ester (7CI, 8CI) (CA INDEX NAME)

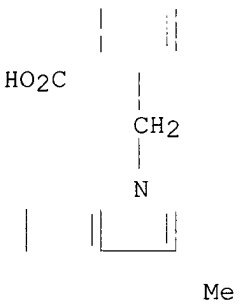


RN 3549-84-6 HCAOLD
CN Benzoic acid, o-(3-benzoyl-2-oxo-1-indolinyl)-, methyl ester (6CI, 7CI, 8CI) (CA INDEX NAME)

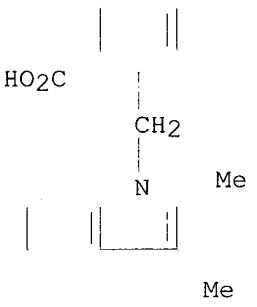


L6 ANSWER 7 OF 7 HCAOLD COPYRIGHT 2002 ACS
AN CA55:5461c CAOLD
TI syntheses and spectroscopic properties in the ultraviolet region of .alpha.-substituted .alpha.-chloroselenophene derivs.
AU Chierici, Luigi; Pappalardo, G.
IT 4098-21-9 22968-46-3 53451-56-2 **108973-42-8** 109842-34-4 112048-62-1 118872-64-3 132725-41-8 **132725-42-9**

IT **108973-42-8 132725-42-9**
RN 108973-42-8 HCAOLD
CN o-Toluic acid, .alpha.-3-methylindol-1-yl- (6CI) (CA INDEX NAME)



RN 132725-42-9 HCAOLD
CN o-Toluic acid, .alpha.-2,3-dimethylindol-1-yl- (6CI) (CA INDEX NAME)



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FILE COVERS 1907 - 22 Apr 2002 VOL 136 ISS 17
FILE LAST UPDATED: 21 Apr 2002 (20020421/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d bib abs hitrn fhitstr retable tot 141

L41 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:566023 HCAPLUS
DN 131:199618
TI Preparation of indole derivatives as **phospholipase** enzyme inhibitors
IN **Seehra, Jasbir S.; Kaila, Neelu; McKew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin**
PA **Genetics Institute**, Inc., USA
SO PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9943651	A2	19990902	WO 1999-US3899	19990224	<--
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	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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	EP 1056719	A2	20001206	EP 1999-908379	19990224	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
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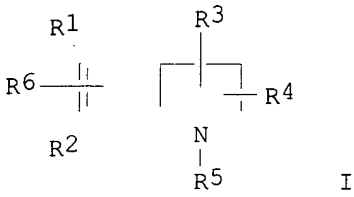
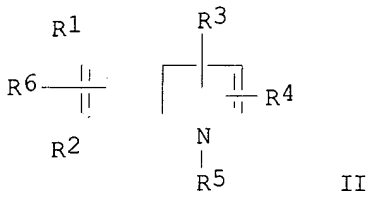
	WO 1999-US3899	W	19990224			

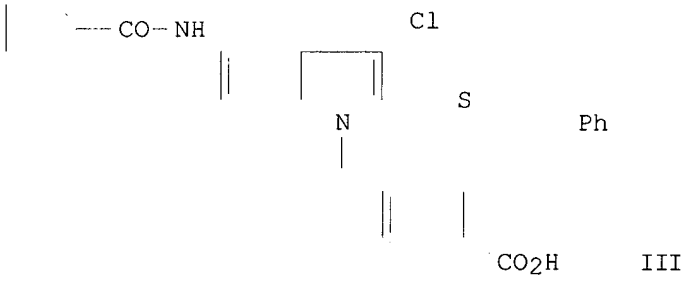
OS MARPAT 131:199618
GI



I



II



III

AB Indole derivs. (I) and (II) [where R1 and R6 = H, halogen, CF3, OH, C1-10 alkyl, S-C1-10 alkyl, C1-10 alkoxy, CN, NO2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amino, amido, carbamido, sulfonyl, etc.; R2 = H, halogen, CF3, OH, C1-10 alkyl, C1-10 alkoxy, CHO, CN, NO2, (un)substituted amino, SO2-C1-6 alkyl; R3 = H, CF3, C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, etc.; R4 = C1-6 alkyl, C1-6 alkoxy, alkylcycloalkyl, acyl, etc.; R5 = (un)substituted carboxylic acid, OPO3H2, SO3H, etc.] and pharmaceutically acceptable salts thereof, were prepd. by several methods. Thus, Et 5-nitroindole-2-carboxylate was C3-chlorinated in DMF. The alc. was formed by redn. of the ester in a two-step process and was then TBDMS-protected. The TBDMS-protected alc. was N-alkylated with Me 4-(bromomethyl)benzoate, the nitro group reduced to the amine over Pt/C, and the compd. reacted with cyclopentylcarbonyl chloride to form the amide. The amide was treated with with Ph3PBr2 in CH2Cl2 to convert the protected alc. to the bromide and then reacted with phenethyl mercaptan in the presence of Cs2CO3 followed by NaOH to yield 4-({3-chloro-5-[(cyclopentylcarbonyl)amino]-2-[(phenethylsulfanyl)methyl]-1H-indol-1-yl}methyl)benzoic acid (III). The title compds. are useful as **phospholipase** enzyme inhibitors, esp. cytosolic **phospholipase** A2 (cPLA2), for treatment of inflammatory conditions, particularly where inhibition of prodn. of prostaglandins, leukotrienes, and PAF are all desired (no data).

IT **9001-84-7, Phospholipase** A2
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(cytosolic; prepn. of indole derivs. as **phospholipase** enzyme inhibitors for treatment of inflammatory conditions)

IT **241493-46-9P 241493-47-0P 241493-48-1P**
241493-51-6P 241493-52-7P 241493-53-8P
241493-54-9P 241493-91-4P 241493-92-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of indole derivs. as **phospholipase** enzyme inhibitors for treatment of inflammatory conditions)

IT **241492-79-5P 241492-80-8P 241492-81-9P**
241493-11-8P 241493-12-9P 241493-13-0P
241493-14-1P 241493-15-2P 241493-30-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole derivs. as **phospholipase** enzyme inhibitors for treatment of inflammatory conditions)

IT **241494-19-9 241494-20-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of indole derivs. as **phospholipase** enzyme inhibitors for treatment of inflammatory conditions)

IT **9001-84-7, Phospholipase** A2
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(cytosolic; prepn. of indole derivs. as **phospholipase** enzyme inhibitors for treatment of inflammatory conditions)

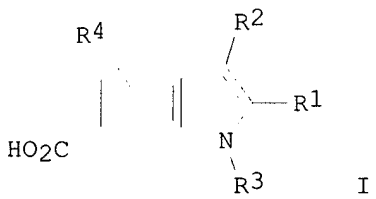
RN 9001-84-7 HCAPLUS
CN Phospholipase A2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L41 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:136882 HCAPLUS
DN 130:182357
TI Solid phase preparation of indole-6-carboxylic acids as estrogenics
IN Collini, Michael David; Ellingboe, John Watson
PA **American Home Products Corporation, USA**
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9909007	A1	19990225	WO 1998-US17236	19980820
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9890258	A1	19990308	AU 1998-90258	19980820
	ZA 9807554	A	20000221	ZA 1998-7554	19980820
PRAI	US 1997-916076	A	19970821		
	WO 1998-US17236	W	19980820		

OS MARPAT 130:182357
GI



I

AB Title compds. [I; R1 = (cyclo)alkyl, phenyl(alkyl), ZNMeCOC6H4(OMe)-4, ZOC6H4(CO2Me)-3; R2 = (cyclo)alkenyl, Ph, 5-methoxy-3,4-dihydronaphthyl, 4-phenylcyclohexenyl, etc.; R3 = H, (carboxy)alkyl, (carboxy)phenyl, etc.; R4 = H, halo, alkyl, alkoxy, etc.; Z = alkylene] were prepd. Thus, resin ester of 3-amino-4-iodobenzoic acid (prepn. given) was alkynylated by

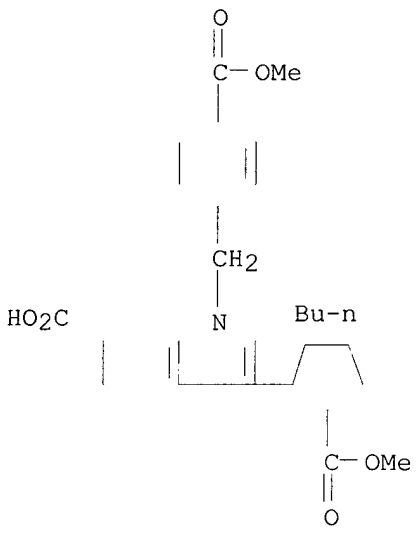
HC.tplbond.CBu and the N-trifluoroacetylated product subjected to alkenylation/cyclization in the presence of 2-methoxycarbonylcyclopentenyl trifluoromethanesulfonate and (Ph3P)4Pd to give, after resin sapon., I (R1 = Bu, R2 = 2-methoxycarbonylcyclopentenyl, R3 = R4 = H). Data for biol. activity of a prepd., I were given.

IT **220690-15-3P 220690-16-4P 220690-17-5P**
220690-18-6P 220690-19-7P 220690-20-0P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(solid phase prepn. of indole-6-carboxylic acids as estrogenics)

IT **220690-15-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(solid phase prepn. of indole-6-carboxylic acids as estrogenics)

RN 220690-15-3 HCAPLUS

CN 1H-Indole-6-carboxylic acid, 2-butyl-3-[2-(methoxycarbonyl)-1-cyclopenten-1-yl]-1-[[4-(methoxycarbonyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



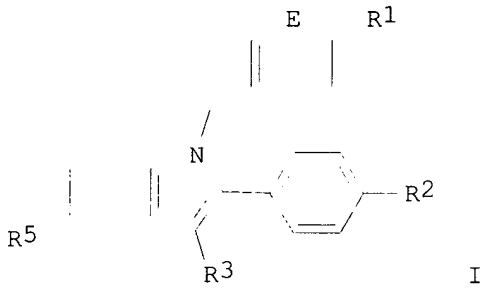
RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Fagnola, M	1997	38	2307	Tetrahedron Letters	HCAPLUS
Kyowa Hakko Kogyo Co, L	1997			EP 0782989 A	HCAPLUS
Pharmacia & Upjohn SPA	1997			WO 9744319 A	HCAPLUS

L41 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:719261 HCAPLUS
DN 129:343412
TI Preparation of 1-benzyl-2-phenylindoles as antithrombotic agents
IN Chirgadze, Nickolay Yuri; Fischer, Matthew Joseph; Harper, Richard Waltz; Lin, Ho-shen; McCowan, Jefferson Ray; Sall, Daniel Jon; Smith, Gerald Floyd; Takeuchi, Kumiko; Wiley, Michael Robert; Zhang, Minsheng
PA Eli Lilly and Co., USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9848797	A1	19981105	WO 1998-US8698	19980430 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9871707	A1	19981124	AU 1998-71707	19980430 <--
	EP 1011666	A1	20000628	EP 1998-918865	19980430 <--
	R: AT, BE, DE, DK, ES, FR, GB, GR, IT, NL, SE, PT, IE, FI				
	JP 2001523254	T2	20011120	JP 1998-547368	19980430 <--
	US 6172100	B1	20010109	US 1999-423125	19991221 <--
PRAI	US 1997-45136P	P	19970430 <--		
	WO 1998-US8698	W	19980430		
OS	MARPAT 129:343412				

GI



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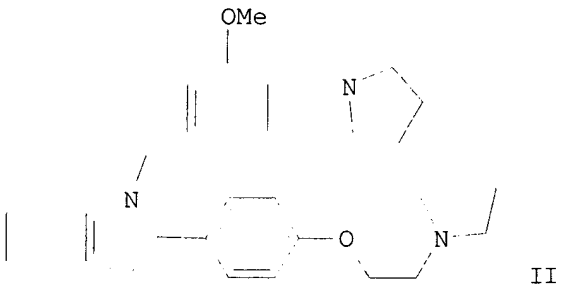


II

AB The title compds. [I; E = CH, CMe, C(OMe), C(halo); R1 = CO2H, (C1-4 alkoxy)carbonyl, CH2OH, etc.; R2 = OCH2Ph, X2(CH2)mNRaRb (wherein X2 = a direct bond, CH2, O, S; m = 1-5; provided that when m = 1, then X2 = a direct bond; Ra, Rb = H, C1-3 alkyl; NRaRb = pyrrolidino, piperidino, morpholino); R2 = X2(CH2)nRf (wherein X2 = a direct bond, CH2, O; n = 1-3; Rf = 5-tetrazolyl, CO2H, (C1-4 alkoxy)carbonyl, CH2OH); R3 = H, Cl, (un)substituted CH2Ph; R5 = H, OH, OMe; provided that at least one of R1 and R2 includes an amino moiety NRsRt or NRaRb] and their salts, useful as thrombin inhibitors, coagulation inhibitors and thromboembolic disorder agents, were prepd. and formulated. Thus, a multi-step synthesis of the title compd. II.(CO2H)2, starting with 4'-hydroxyacetophenone and

2-(1-pyrrolidinyl)ethanol, was described. Compds. I are effective at 0.01-1000 mg/kg/day.

IT **215584-18-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-benzyl-2-phenylindoles as antithrombotic agents)

IT **215584-17-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 1-benzyl-2-phenylindoles as antithrombotic agents)

IT **215584-38-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 1-benzyl-2-phenylindoles as antithrombotic agents)

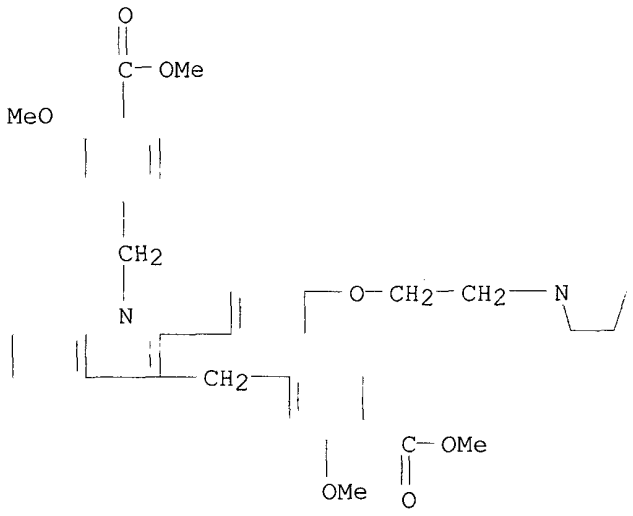
IT **215584-18-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-benzyl-2-phenylindoles as antithrombotic agents)

RN 215584-18-2 HCAPLUS

CN Benzoic acid, 4,4'-[[2-[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]-1H-indole-1,3-diyl]bis(methylene)]bis[2-methoxy-, dimethyl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)

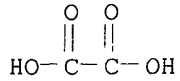
CM 1

CRN 215584-17-1
CMF C40 H42 N2 O7



CM 2

CRN 144-62-7
CMF C2 H2 O4



L41 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:208560 HCAPLUS
DN 128:257331
TI Preparation of 3-acylpyrrole- and -indole-2-carboxylic acids as inhibiting agents of cytosolic **phospholipase** A2
IN Lehr, Matthias
PA Merckle G.m.b.H., Germany
SO Ger. Offen., 14 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19638408	A1	19980326	DE 1996-19638408	19960919 <--

OS MARPAT 128:257331
GI

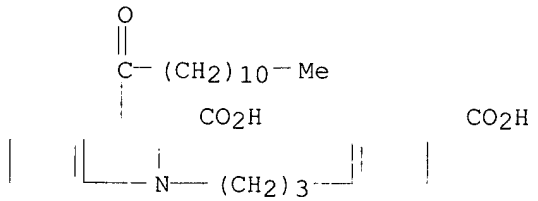
AB The title compds. [I and II; R1 = 7-carboxyheptyl 8-carboxyoctyl, 9-carboxynonyl, 10-carboxydecyl, 11-carboxyundecyl, 3-(carboxyphenyl)propyl, 2-(carboxyphenoxy)ethyl; R2 = C9-13 alkyl] and their pharmaceutically acceptable salts were prepd., e.g., by N-alkylation of the corresponding pyrrole- and indolecarboxylate ester precursors with alkyl halides X(CH2)nCO2R5, X(CH2)2OC6H4CO2R5 or X(CH2)3C6H4CO2R5 [X = halo, esp. Br; R5 = Me, Et, Pr, Bu, Me(CH2)4, Me(CH2)5, Me3C, Ph, PhCH2; n = 7-11] followed by ester hydrolysis. For example, 1-(8-carboxyoctyl)-3-dodecanoylindole-2-carboxylic acid (III) (m. 110-111.degree.) was prepd. in 9% yield by N-alkylation of indole-2-carboxylic acid Et ester with Br(CH2)8CO2Et in the presence of Me3COK in DMSO, acylation of the intermediate with Me(CH2)10CO2H in the presence of polyphosphoric acid and (CF3CO)2O, sapon. of esters with aq.-ethanolic KOH and acidification with dild. HCl. III inhibited cytosolic **phospholipase** A2 with IC50 0.5 .mu.M, vs. 8 .mu.M for 1-methyl-3-octadecanoyl-2-carboxylic acid, a previous art **PLA2** inhibitor.

IT **205106-44-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-acylpyrrole- and -indole-2-carboxylic acids as inhibiting agents of cytosolic **phospholipase** A2)

IT **9001-84-7**, **Phospholipase** A2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of 3-acylpyrrole- and -indole-2-carboxylic acids as inhibiting agents of cytosolic **phospholipase** A2)

IT **205106-44-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-acylpyrrole- and -indole-2-carboxylic acids as inhibiting agents of cytosolic **phospholipase** A2)

RN 205106-44-1 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[3-(4-carboxyphenyl)propyl]-3-(1-oxododecyl)- (9CI) (CA INDEX NAME)



L41 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:112340 HCAPLUS
DN 128:167350
TI Preparation of acylpyrrole- and acylindoledicarboxylic acids as **phospholipase** A2 inhibitors
IN Lehr, Matthias
PA Merckle G.m.b.H., Germany; Lehr, Matthias
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805637	A1	19980212	WO 1997-EP3842	19970717 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9737679	A1	19980225	AU 1997-37679	19970717 <--
	EP 923546	A1	19990623	EP 1997-934481	19970717 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000515529	T2	20001121	JP 1998-507515	19970717 <--
	NO 9900413	A	19990128	NO 1999-413	19990128 <--
	KR 2000029658	A	20000525	KR 1999-700734	19990129 <--
	US 6310217	B1	20011030	US 1999-240148	19990129 <--
PRAI	DE 1996-19631102	A	19960801 <--		
	WO 1997-EP3842	W	19970717 <--		

OS MARPAT 128:167350
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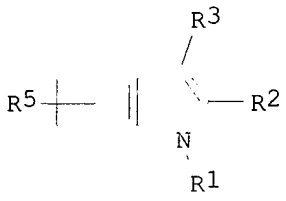


I

AB Title compds. [e.g., I; R1 = Y1ArY2Y3; R2 = carboxy(alkyl), alkoxycarbonyl(alkyl), carbamoyl(alkyl), etc.; R3 = alkanoyl, aroyl, etc.; R5 = H or .gtoreq.1 of halo, alkyl, alkoxy, etc.; Y1,Y2 = alk(en)ylene, etc.; Y3 = CO2H, alkoxycarbonyl, CONH2, etc.; Ar = (un)substituted arylene] were prepd. Thus, Et pyrrole-2-carboxylate was acylated and the product N-alkylated by (E)-4-(BrH2C)C6H4CH:CHCO2Et to give, after sapon., I [R1 = (E)-H2CC6H4(CH:CHCO2Et)-4, R2 = CO2H, R3 = dodecanoyl, R5 = H]. Data for biol. activity of title compds. were given.

IT **9001-84-7, Phospholipase** A2
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(mediated disorders; treatment; prepn. of acylpyrrole- and acylindoledicarboxylic acids as **phospholipase** A2 inhibitors)

IT **192182-33-5P 192182-35-7P 192182-37-9P 192182-39-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylpyrrole- and acylindoledicarboxylic acids as **phospholipase** A2 inhibitors)

IT **203111-22-2P 203111-24-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of acylpyrrole- and acylindoledicarboxylic acids as **phospholipase** A2 inhibitors)

IT **9001-84-7, Phospholipase** A2
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(mediated disorders; treatment; prepn. of acylpyrrole- and acylindoledicarboxylic acids as **phospholipase** A2 inhibitors)

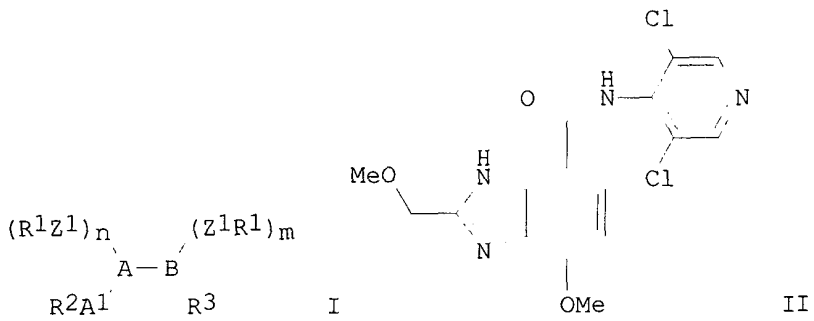
RN 9001-84-7 HCAPLUS
CN Phospholipase A2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L41 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:31305 HCAPLUS
DN 128:102087
TI Substituted azabicyclic compounds and their use as inhibitors of the production of TNF and cyclic AMP phosphodiesterase
IN Cox, Paul Joseph; Bower, Shelley; Aldous, David John; Astles, Peter Charles; McGarry, Daniel Gerard; Hulme, Christopher; et al.
PA Regan, John Robinson, UK; Huang, Fu-Chih; et al.; Rhone-Poulenc Rorer Ltd.; Cox, Paul Joseph; Bower, Shelley
SO PCT Int. Appl., 355 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9748697	A1	19971224	WO 1997-GB1639	19970619 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2258728	AA	19971224	CA 1997-2258728	19970619 <--
AU 9731026	A1	19980107	AU 1997-31026	19970619 <--
ZA 9705446	A	19981221	ZA 1997-5446	19970619 <--
EP 934307	A1	19990811	EP 1997-926148	19970619 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000509719	T2	20000802	JP 1998-502503	19970619 <--

US 6303600 B1 20011016 US 1998-216392 19981218 <--
PRAI GB 1996-12760 A 19960619 <--
US 1996-23047P P 19960802 <--
WO 1997-GB1639 W 19970619 <--
OS MARPAT 128:102087
GI

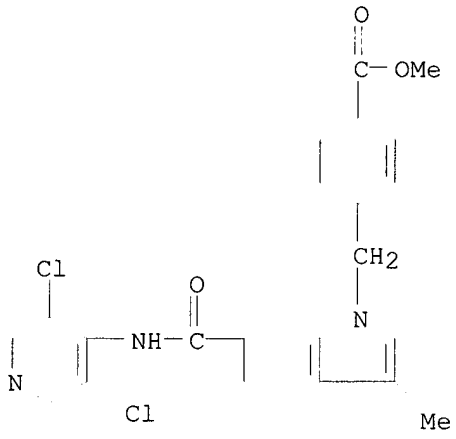


AB The invention is directed to physiol. active compds. of formula I [wherein AB = fused bicyclic ring system, of approx. 10-13 ring members, wherein A = azaheterocycle ring and B = azaheteroaryl or optionally halo-substituted benzene ring; R1 = H, (hydroxy- or halo-substituted) alkyl, and also alkenyl, alkynyl, or CHO when Z1 = bond; R2 = H, alkenyl, alkoxy, alkyl, aryl, aryloxy, cyano, etc.; R3 = wide variety of sidechains and functional groups; A1 = bond, (un)substituted alkylene, alkenylene, alkynylene; Z1 = bond, O, S, NH; m, n = 0, 1; provided that (n+m) = 1] and their N-oxides, prodrugs, and pharmaceutically acceptable salts and solvates. I inhibit the prodn. or physiol. effects of TNF, and inhibit cAMP phosphodiesterase (PDE IV). The invention is also directed to pharmaceutical compns. comprising I, their pharmaceutical use, and methods for their prepn. For instance, 7-methoxy-2-(methoxymethyl)-3H-benzimidazole-4-carboxylic acid (prepn. given) was treated with O-benzotriazol-1-yl-N,N,N',N'-bis(tetramethylene)uronium tetrafluoroborate to give the 1-benzotriazolyl ester, which was amidated with 4-amino-3,5-dichloropyridine in THF (after treatment of the latter with Na diethylaluminate) to give the title compd. II. Compds. I had IC50 of 10-5 to 10-10 M against guinea pig macrophage PDE IV, with 50- to 10,000-fold selectivity for PDE IV vs. PDE I, II, III, or V. The compds. also inhibited antigen-induced bronchoconstriction in rats by up to 89% at oral doses of 10 mg/kg.

IT **201286-09-1P 201286-14-8P 201286-15-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of azabicyclic compds. as inhibitors of TNF prodn. and PDE IV)

IT **201286-09-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of azabicyclic compds. as inhibitors of TNF prodn. and PDE IV)

RN 201286-09-1 HCAPLUS
CN Benzoic acid, 4-[[6-[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-3-methyl-1H-indol-1-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:510146 HCAPLUS
DN 127:121734
TI Preparation of benzimidazolylmethyl- and indolylmethylphenylacetamides as antiarteriosclerotics.
IN Connell, Richard; Goldmann, Siegfried; Mueller, Ulrich; Lohmer, Stefan; Bischoff, Hilmar; Denzer, Dirk; Gruetzmann, Rudi; Wohlfeil, Stefan
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 55 pp.
CODEN: EPXXDW
DT **Patent**
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 779276	A1	19970618	EP 1996-119320	19961203 <--
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	DE 19546919	A1	19970619	DE 1995-19546919	19951215 <--
	US 6034115	A	20000307	US 1996-761922	19961209 <--
	JP 09328466	A2	19971222	JP 1996-352419	19961213 <--
	US 6235770	B1	20010522	US 1999-435544	19991108 <--
	US 2002028940	A1	20020307	US 2001-840419	20010423 <--
PRAI	DE 1995-19546919	A	19951215	<--	
	US 1996-761922	A3	19961209	<--	
	US 1999-435544	A3	19991108		

OS MARPAT 127:121734
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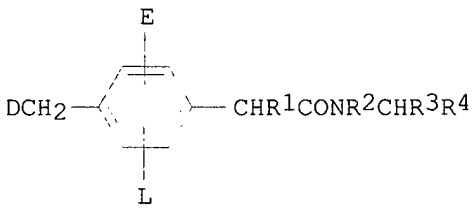


I

AB Title compds. [I; D = indolyl, benzimidazolyl, imidazopyridyl; E, L = H, halo, CF3, OH, CO2H, alkyl, alkoxy, alkoxycarbonyl; R1 = cycloalkyl,

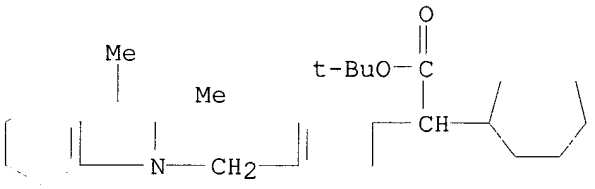
alkyl, (substituted) Ph; R2 = H, alkyl; R3 = H, alkyl, cycloalkyl, (substituted) Ph, heterocyclyl; R4 = CH2OH, CH2O2R12; R12 = H, alkyl, (substituted) Ph], were prepd. Thus, 2(RS)-2-[4-(2-phenyl-1H-benzimidazol-1-ylmethyl)phenyl]-2-cyclopentylacetic acid (prepn. given) in DMF contg. Et3N was treated with MeSO2Cl, dimethylaminopyridine, and (R)-phenylglycinol at -30.degree. to room temp. to give 99% 2(RS)-2-[4-(2-phenyl-1H-benzimidazol-1-ylmethyl)phenyl]-2-cyclopentylacetic acid (R)-phenylglycinolamide. I inhibited ApoB-assocd. lipoprotein release from liver cells with IC50 = 1.5-1010.1 nM.

IT **192585-32-3P 192585-35-6P 192585-36-7P**
192585-42-5P 192585-68-5P 192585-71-0P
192585-72-1P 192585-79-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of benzimidazolylmethyl- and indolylmethylphenylacetamides as antiarteriosclerotics)

IT **192585-32-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of benzimidazolylmethyl- and indolylmethylphenylacetamides as antiarteriosclerotics)

RN 192585-32-3 HCAPLUS

CN Cycloheptaneacetic acid, .alpha.-[4-[(2,3-dimethyl-1H-indol-1-yl)methyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:499100 HCAPLUS

DN 127:190643

TI Preparation of nitrogen-containing compounds as intimal thickening inhibitors

IN Sato, Atsushi; Asao, Tetsuji; Hagiwara, Yuichi; Kitade, Makoto; Yamazaki, Yasundo

PA Taiho Pharmaceutical Co., Ltd., Japan; Sato, Atsushi; Asao, Tetsuji; Hagiwara, Yuichi; Kitade, Makoto; Yamazaki, Yasundo

SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2

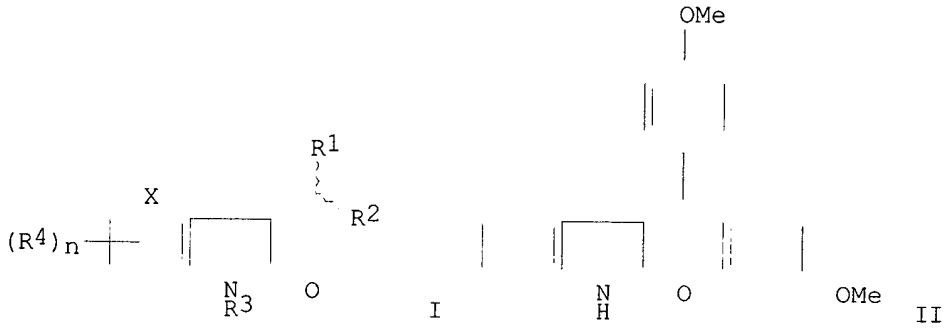
DT **Patent**

LA Japanese

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9725986	A1	19970724	WO 1997-JP65	19970116 <--
W: AU, CA, FI, HU, JP, KR, NO, RU, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2214759	AA	19970724	CA 1997-2214759	19970116 <--
AU 9713986	A1	19970811	AU 1997-13986	19970116 <--
AU 708167	B2	19990729		
EP 815859	A1	19980107	EP 1997-900424	19970116 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 3000300	B2	20000117	JP 1997-521937	19970116 <--
RU 2145852	C1	20000227	RU 1997-117350	19970116 <--
US 5977130	A	19991102	US 1997-913237	19970910 <--
NO 9704280	A	19971111	NO 1997-4280	19970916 <--

PRAI JP 1996-5693 A 19960117 <--
WO 1997-JP65 W 19970116 <--
OS MARPAT 127:190643
GI



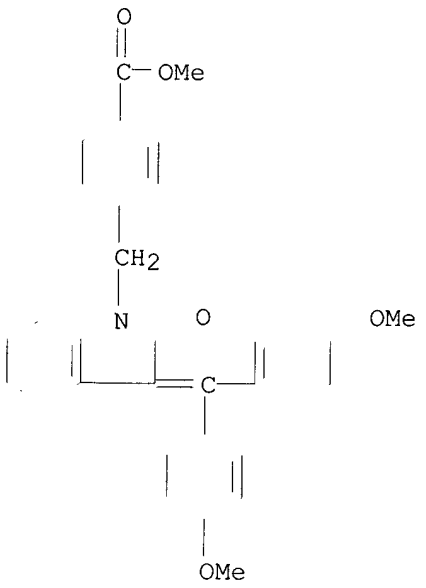
AB The title compds. (I; R1 = H, Ph optionally substituted by lower alkyl, alkoxy, or lower alkylaminoalkoxy, OH, amino, lower alkylamino, halo, or pyridyl optionally substituted by lower alkyl, alkoxy, or lower alkylaminoalkoxy, OH, amino, lower alkylamino, halo, lower alkoxycarbonyl or carboxy; R2 = H, optionally substituted Ph, or pyridyl optionally substituted by lower alkyl, lower alkoxy, lower alkylamino-alkoxy, hydroxy, amino, lower alkylamino, halo, lower alkoxycarbonyl or CO2H; R3 = H, sents H optionally substituted lower alkyl, benzyl or benzenesulfonyl, or acyl; R4 = H, lower alkoxy, halo, amino, lower alkylamino, carboxy, lower alkoxycarbonyl, optionally substituted phenylcarbamoyl, or trifluoromethyl; X = H, CH, N; n = 0-4; the double line composed of dotted and solid lines means that this bond is either a single or a double bond). I show excellent effects of inhibiting intimal thickening and thus useful in preventing, treating and relieving proliferative vascular lesions such as vascular reconstriction after percutaneous transluminal coronary recanalization, arterial sclerosis, peripheral embolism and angiitis. Thus, oxyindole was refluxing with 4,4'-dimethoxybenzophenone in the presence of NaH in THF to give 85% the title compd. II, which at 30 mg/kg showed 33.2% rat intimal thickening inhibitory activity. Formulation of I is also presented.

IT **193620-94-9P 193620-97-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nitrogen-contg. compds. as intimal thickening inhibitors)

IT **193620-94-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nitrogen-contg. compds. as intimal thickening inhibitors)

RN 193620-94-9 HCAPLUS

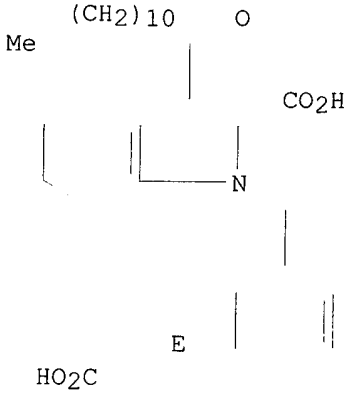
CN Benzoic acid, 4-[[3-[bis(4-methoxyphenyl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:483378 HCAPLUS
DN 127:90133
TI Synthesis, Biological Evaluation, and Structure-Activity Relationships of 3-Acylindole-2-carboxylic Acids as Inhibitors of the Cytosolic **Phospholipase** A2
AU Lehr, Matthias
CS Institute of Pharmacy and Food Chemistry, Ludwig-Maximilians-University, Munich, D-80333, Germany
SO J. Med. Chem. (**1997**), 40(17), 2694-2705
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB 3-Acylindole-2-carboxylic acid derivs. were prepd. and evaluated for their ability to inhibit the cytosolic **phospholipase** A2 of intact bovine platelets. To define the structural requirements for enzyme inhibition, the carboxylic acid group, the acyl residue, and the moiety in position 1 were systematically modified. Furthermore, different substituents were introduced into the Ph part of the indole. Replacement of the carboxylic acid group in position 2 of the indole with an acetic or propionic acid substituent led to a decrease of inhibitory potency. Enzyme inhibition was optimal when the acyl residue in position 3 had a length of 12 or more carbons. Conformational restriction of the acyl residue did not influence activity. Introduction of alkyl chains at position 1 of the indole with 8 or more carbons resulted in a loss of activity. However, replacing the .omega.-Me group of such compds. with a carboxylic acid moiety increased inhibitory potency significantly. Among the tested indole derivs., 1-[2-(4-carboxyphenoxy)ethyl]-3-dodecanoylindole-2-carboxylic acid had the highest potency. With an IC50 of 0.5 .mu.M it was about 20-fold more active than the std. cPLA2 inhibitor arachidonyl trifluoromethyl ketone (IC50: 11 .mu.M).
IT **192182-33-5P 192182-35-7P 192182-37-9P 192182-39-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and structure-activity relationships of acylindolecarboxylates as inhibitors of **phospholipase** A2)

IT **9001-84-7, Phospholipase** A2
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. and structure-activity relationships of acylindolecarboxylates as inhibitors of **phospholipase** A2)
IT **192182-33-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and structure-activity relationships of acylindolecarboxylates as inhibitors of **phospholipase** A2)
RN 192182-33-5 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[[3-(2-carboxyethenyl)phenyl]methyl]-3-(1-oxododecyl)-, (E)- (9CI) (CA INDEX NAME)

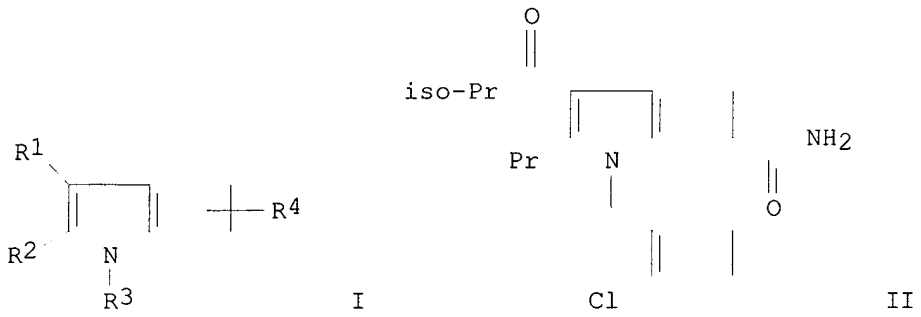
Double bond geometry as shown.



L41 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:746234 HCAPLUS
DN 126:18786
TI Indole derivatives as cGMP-PDE inhibitors
IN Oku, Teruo; Sawada, Kozo; Kuroda, Akio; Ohne, Kazuhiko; Nomoto, Atsushi; Hosogai, Naomi; Nakajima, Yoshimitsu; Nagashima, Akira; Sogabe, Keizo; Amura, Kouichi
PA Fujisawa Pharmaceutical Co, Ltd., Japan
SO PCT Int. Appl., 211 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	WO 9632379	A1	19961017		WO 1996-JP892	19960402	<--
	CA 2217707	AA	19961017		CA 1996-2217707	19960402	<--
	AU 9651234	A1	19961030		AU 1996-51234	19960402	<--
	AU 713460	B2	19991202				
	EP 820441	A1	19980128		EP 1996-907750	19960402	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI						
	CN 1187812	A	19980715		CN 1996-194691	19960402	<--
	JP 11503445	T2	19990326		JP 1996-530864	19960402	<--
	ZA 9602859	A	19961011		ZA 1996-2859	19960410	<--
	TW 420663	B	20010201		TW 1996-85104519	19960416	<--
	US 6069156	A	20000530		US 1997-930597	19971210	<--
PRAI	GB 1995-7432	A	19950410	<--			
	GB 1995-12560	A	19950621	<--			
	GB 1995-16136	A	19950807	<--			
	AU 1996-8294	A	19960227	<--			
	WO 1996-JP892	W	19960402	<--			

OS MARPAT 126:18786
GI



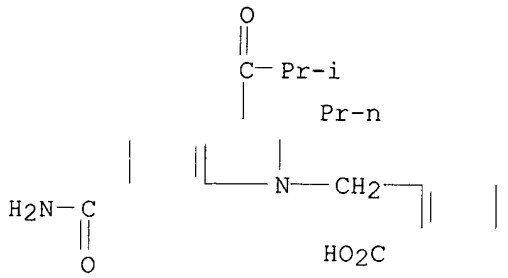
AB The invention relates to new indole derivs. I and their pharmaceutically acceptable salts [wherein R1 = H, halo, NO2, CO2H, protected CO2H, acyl, (un)substituted alk(en)yl, etc.; R2 = H, halo, alkenyl, acyl, (un)substituted alkyl, etc.; R3 = (un)substituted alk(en)yl where the substituent is oxo, (un)substituted aryl, or heterocyclyl; R4 = CO2H, protected CO2H, acyl, cyano, amino, halo, etc.; R1 and R2 may form 4- to 7-membered carboxylic ring (un)substituted with oxo]. I are cyclic nucleotide-PDE inhibitors (specifically cGMP-PDE), and are useful for treating and preventing a variety of conditions, including angina, hypertension, renal failure, atherosclerosis, stroke, asthma, impotence, diabetic complications, and glaucoma. Almost 300 compds. I and numerous intermediates were prepd. For example, Me 3-isobutyryl-2-propylindole-6-carboxylate (prepn. given) was N-benzylated by 2-chlorobenzyl bromide using NaH in DMF. The product underwent sapon. with NaOH in aq. EtOH, followed by amidation of the resultant acid using EDC, HOBt, and aq. NH3, to give title amide II. II inhibited human platelet cGMP-PDE in vitro with IC50 <100 nM. I were also active in a variety of other bioassays, including relaxation of isolated rat aorta, inhibition of vascular smooth muscle cell proliferation, inhibition of vasopressin-induced vasospasm, the cyclosporin and FK506 nephritis models, the diabetic glomerulosclerosis model, and several animal impotence models.

IT **184148-89-8P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole derivs. as cGMP-PDE inhibitors)

IT **184148-12-7P 184150-10-5P 184150-66-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole derivs. as cGMP-PDE inhibitors)

IT **184148-89-8P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indole derivs. as cGMP-PDE inhibitors)

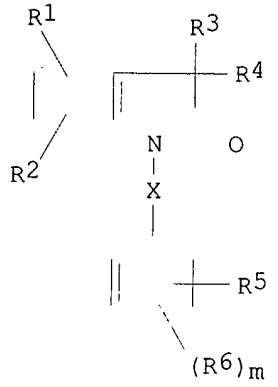
RN 184148-89-8 HCAPLUS
CN Benzoic acid, 2-[[6-(aminocarbonyl)-3-(2-methyl-1-oxopropyl)-2-propyl-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)



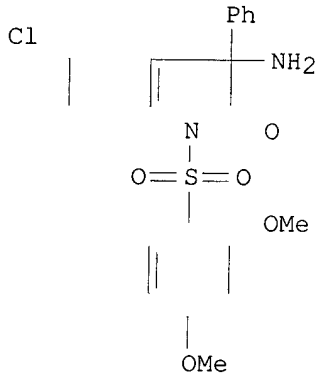
L41 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:858609 HCAPLUS
DN 123:256516
TI Indol-2-one derivatives substituted in the 3-position by a nitrogenous group, their preparation, and pharmaceutical compositions containing them as vasopressin and/or oxytocin receptor ligands.
IN Wagnon, Jean; Tonnerre, Bernard; Di Malta, Alain; Roux, Richard; Amiel, Marie-Sophie; Serradeil-Legal, Claudine
PA Sanofi, Fr.
SO Fr. Demande, 70 pp.
CODEN: FRXXBL
DT **Patent**
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2714378	A1	19950630	FR 1993-15638	19931224 <--
	FR 2714378	B1	19960315		
	WO 9518105	A1	19950706	WO 1994-FR1528	19941223 <--
	W: JP, LT, SI, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 687251	A1	19951220	EP 1995-905164	19941223 <--
	EP 687251	B1	20020227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08507092	T2	19960730	JP 1994-517812	19941223 <--
	AT 213727	E	20020315	AT 1995-905164	19941223 <--
	US 5594023	A	19970114	US 1995-500924	19950731 <--
	US 5773612	A	19980630	US 1996-640080	19960430 <--
PRAI	FR 1993-15638	A	19931224 <--		
	WO 1994-FR1528	W	19941223 <--		
	US 1995-500924	A3	19950731 <--		

OS CASREACT 123:256516; MARPAT 123:256516
GI



I



II

AB Title compds. I [R1, R2 = H, halo, alkyl, alkoxy, CF3; R3 = alkyl, cycloalkyl, (di)alkylcyclohexyl, (un)substituted Ph; R4 = N3, alkylsulfonamido, (un)substituted phenylsulfonamido, dimethylaminosulfonamido, (un)substituted NH2, heterocyclyl; R5 = H, R6; R6 = halo, alkyl, CF3, cyano, (di)(alkyl)aminomethyl, NO2, (un)substituted amino, carboxy, carbamoyl, acyl, etc.; X = SO2, CH2; m = 1, and sometimes 2-4] and salts are claimed, and approx. 100 examples are given. The compds. have affinity for vasopressin and/or oxytocin receptors, and are useful for treating disorders of the central and peripheral nervous, cardiovascular, renal, and gastric systems, as well as sexual disorders. For example, bromination of 5-chloro-1,3-dihydro-3-phenylindol-2-one with Br2 in CCl4 gave the 3-bromo deriv., which reaced with anhyd. NH3 in Et2O to give the 3-amino deriv. Treatment of this with NaH in DMF and then with 2,4-(MeO)2C6H3SO2Cl yielded title compd. II. In a test for inhibition of binding of [3H]-arginine-vasopressin to bovine renal V2 receptors, I had IC50 down to 10-9 M.

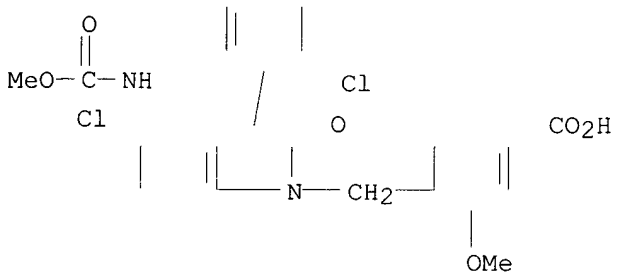
IT **169040-71-5P 169040-72-6P 169040-73-7P 169040-74-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of indolone derivs. as vasopressin and/or oxytocin receptor ligands)

IT **169040-12-4P 169040-13-5P 169040-16-8P**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of indolone derivs. as vasopressin and/or oxytocin receptor ligands)

IT **169040-71-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of indolone derivs. as vasopressin and/or oxytocin receptor ligands)

RN 169040-71-5 HCAPLUS

CN Benzoic acid, 4-[[5-chloro-3-(2-chlorophenyl)-2,3-dihydro-3-[(methoxycarbonyl)amino]-2-oxo-1H-indol-1-yl]methyl]-3-methoxy- (9CI) (CA INDEX NAME)



L41 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:661173 HCAPLUS
DN 124:8801
TI Substituted indole-, indene-, pyranoindole- and tetrahydrocarbazolealkanoic acid derivatives as inhibitors of **PLA2** and lipoxygenase
IN Musser, John H.; Kreft, Anthony F., III; Failli, Amedeo A.; Demerson, Christopher A.; Shah, Uresh S.; Nelson, James A.
PA **American Home Products Corporation, USA**
SO U.S., 35 pp. Cont.-in-part of U.S. 5,229,516.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 5420289	A	19950530		US 1993-29199	19930310 <--
	CA 2090042	AA	19910428		CA 1990-2090042	19901027 <--
	US 5229516	A	19930720		US 1992-911434	19920710 <--
PRAI	US 1989-428260		19891027	<--		
	US 1990-596134		19901011	<--		
	US 1992-911434		19920710	<--		
	CA 1990-2070422		19901027	<--		

OS MARPAT 124:8801
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This invention relates to substituted indole derivs. A(CH2)nOB wherein A = I or II wherein R1 is hydrogen, lower alkyl, Ph or Ph substituted with trifluoromethyl; R2 is hydrogen or lower alkyl; or R1 and R2 taken together form a benzene ring; R3 is hydrogen or lower alkyl; n is 1-2; B is III-VII wherein R4 is, e.g., CO2R2, m is 0-3; R5 is A(CH2)nOC6H4 or Ph or Ph substituted by halo, lower alkylthio, lower alkylsulfinyl or lower alkylsulfonyl; R6 is A(CH2)nO or halo; R7 is lower alkyl; Y is CH2 or O; R8 is lower alkyl or (CH2)mCO2R3 ; R9 is COR10 or (CH2)oR10, o is 1-4; R10 is lower alkyl, Ph, Ph substituted with carboxy, halo, lower alkyl, loweralkylthio or loweralkylsulfinyl; naphthyl, pyridyl, furanyl, quinolinyl, or 2-R14-thiazolyl; R11 is lower alkyl or phenyl; R12 is hydrogen or loweralkylcarbonyl R13 is hydrogen, hydroxy, lower alkyl or lower alkoxy; R14 is Ph or halophenyl; Z2 is hydrogen, lower alkyl or N(CH3)OH; and the pharmacol. acceptable salts thereof possessing lipoxygenase inhibitory, **phospholipase** A2 inhibitory and leukotriene antagonist activity, which are useful as anti-inflammatory, antiallergic and cytoprotective agents. Thus, e.g., condensation of

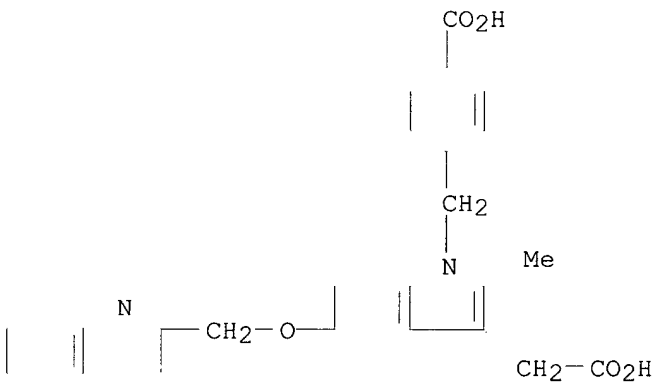
2-methyl-5-(2-quinolinylmethoxy)indene-3-acetic acid Et ester (prepn. given, mixt. of endo and exo isomers) with p-chlorobenzaldehyde afforded 3-[(4-chlorophenyl)methylene]-2-methyl-6-(2-quinolinylmethoxy)-3H-indene-1-acetic acid [VIII, Q = 2-quinolinylmethyl, mixt. of Z (major) and E (minor) isomers]. The specificity of action of **PLA2** inhibitors can be detd. by the activity of test compds. to inhibit the synthesis of LTB4 by rat glycogen-elicited polymorphonuclear leukocytes (PMN) in the presence of exogenous substrate: VIII demonstrated 96% inhibition at 10 mM. VIII also inhibited the synthesis of the arachidonic acid cyclooxygenase oxidn. product PGE2 with 81% inhibition at 10 mM. VIII inhibited the release of arachidonic acid from an arachidonic acid-contg. substrate by the action of **phospholipase** A2 enzyme from human synovial fluid with IC50 = 9.7 mM. Further assays demonstrated that the compds. of the invention exerted an inhibitory effect on both the lipoxygenase pathway and the cyclooxygenase pathway and have significant leukotriene (LTD4) antagonist activity. The compds. of the invention inhibited the acute inflammatory response and inhibited 5-lipoxygenase in human whole blood.

IT **135872-88-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted indole-, indene-, pyranoindole- and tetrahydrocarbazolealkanoic acid derivs. as inhibitors of **PLA2** and lipoxygenase)

IT **9001-84-7, Phospholipase** A2
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(substituted indole-, indene-, pyranoindole- and tetrahydrocarbazolealkanoic acid derivs. as inhibitors of **PLA2** and lipoxygenase)

IT **135872-88-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted indole-, indene-, pyranoindole- and tetrahydrocarbazolealkanoic acid derivs. as inhibitors of **PLA2** and lipoxygenase)

RN 135872-88-7 HCAPLUS
CN 1H-Indole-3-acetic acid, 1-[(4-carboxyphenyl)methyl]-2-methyl-5-(2-quinolinylmethoxy)- (9CI) (CA INDEX NAME)



L41 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:298483 HCAPLUS
DN 120:298483

TI Substituted indole-, indene-, pyranoindole- and tetrahydrocarbazole-alkanoic acid derivatives as inhibitors of **phospholipase** A2 and lipoxygenase

IN Musser, John H.; Kreft, Anthony F., III; Failli, Amedeo A.; Demerson, Christopher A.; Shah, Uresh S.; Nelson, James A.

PA **American Home Products Corp., USA**

SO U.S., 32 pp. Cont.-in-part of U.S. Ser. No. 596,134, abandoned. CODEN: USXXAM

DT **Patent**

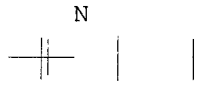
LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5229516	A	19930720	US 1992-911434	19920710 <--
	CA 2070422	AA	19910428	CA 1990-2070422	19901027 <--
	CA 2090042	AA	19910428	CA 1990-2090042	19901027 <--
	HU 63407	A2	19930830	HU 1992-1383	19901027 <--
	US 5420289	A	19950530	US 1993-29199	19930310 <--
	WO 9401407	A2	19940120	WO 1993-US6441	19930707 <--
	WO 9401407	A3	19940303		
	W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9346694	A1	19940131	AU 1993-46694	19930707 <--
PRAI	US 1989-428260		19891027 <--		
	US 1990-596134		19901011 <--		
	CA 1990-2070422		19901027 <--		
	US 1992-911434		19920710 <--		
	WO 1993-US6441		19930707 <--		

OS MARPAT 120:298483

GI

Q= 

AB The title compds. A(CH2)nOB [A = Q; B = (un)substituted indenonyl, (un)substituted indolyl, etc.; n = 1-2], useful as antiinflammatory agents which possess leukotriene antagonistic activity, are prepd. Thus, 3-[(4-chlorophenyl)methylene]-[2-methyl-6-(2-quinolinylmethyoxy)]-3H-indene-1-acetic acid (Z configuration), prepd. from 4-methoxybenzaldehyde in 7 steps, demonstrated 81% inhibition of PGE2 at 10 .mu.M.

IT **9001-84-7, Phospholipase** A2
RL: RCT (Reactant)
(inhibition of, substituted heterocyclo- and indenealkanoates for)

IT **135872-88-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and lipoxygenase and **phospholipase** A2 inhibitory activity of)

IT **9001-84-7, Phospholipase** A2
RL: RCT (Reactant)
(inhibition of, substituted heterocyclo- and indenealkanoates for)

RN 9001-84-7 HCAPLUS

CN Phospholipase A2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L41 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2002 ACS

AN 1991:535935 HCAPLUS
DN 115:135935
TI Preparation of indole-, indene-, pyranoindole- and tetrahydrocarbazolealkanoic acid derivatives as inhibitors of **phospholipase** A2 and lipoxygenase
IN Musser, John Henry; Kreft, Anthony Frank, III; Failli, Amedeo Arturo; Demerson, Christopher Alexander; Shah, Uresh Shantilal; Nelson, James Albert
PA **American Home Products Corp., USA**
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9106537	A2	19910516	WO 1990-US6251	19901027 <--
	WO 9106537	A3	19911017		
	W: AU, BR, CA, FI, HU, JP, KR, SU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	CA 2070422	AA	19910428	CA 1990-2070422	19901027 <--
	CA 2090042	AA	19910428	CA 1990-2090042	19901027 <--
	AU 9177404	A1	19910531	AU 1991-77404	19901027 <--
	AU 643996	B2	19931202		
	EP 502106	A1	19920909	EP 1991-900547	19901027 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	BR 9007790	A	19920915	BR 1990-7790	19901027 <--
	JP 05502222	T2	19930422	JP 1991-500787	19901027 <--
	HU 63407	A2	19930830	HU 1992-1383	19901027 <--
	FI 9201865	A	19920424	FI 1992-1865	19920424 <--
PRAI	US 1989-428260		19891027 <--		
	US 1990-596134		19901011 <--		
	CA 1990-2070422		19901027 <--		
	WO 1990-US6251		19901027 <--		

OS MARPAT 115:135935
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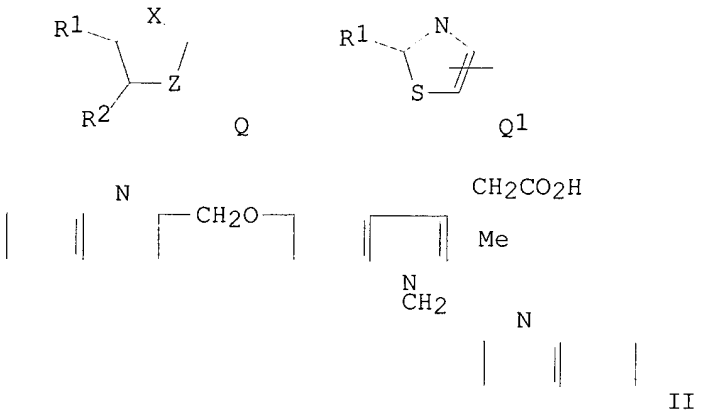


AB A(CH2)nOB [I; A = C4-8 alkyl, PhOCH2CH2, PhOC6H4, Q, Q1; R1 = H, alkyl, Ph, C6H4CF3; R2 = H, alkyl; R1R2 = benzene; X = N, R3C, R3 = H, alkyl; Z = R3C:CR3, R3C:N, N:CR3, NR3, O, S; n = 1, 2; B = substituted indanyl, substituted carbazolyl, substituted pyranoindolyl, etc.] and a salt thereof, are prepd. I are useful as antiinflammatory agents and possess leukotriene antagonistic activity. To a stirred suspension of NaH in DMF at 0.degree. was added 5-hydroxy-2-methyl-1H-indole-3-acetic acid followed

after 1 h by 2-(chloromethyl)quinoline. The reaction mixt. allowed to warm at room temp. with stirring overnight and the pH adjusted to 5 with HCl to give the indoleacetic acid (II) which at 10 .mu.M in vitro gave 47% inhibition of **phospholipase** A2 (**PLA2**) from semi-purified human platelet ext., and 30% of **PLA2** from purified human synovialfluid.

IT **9001-84-7, Phospholipase** A2
RL: USES (Uses)
(inhibitors, substituted heterocycle- and indene alkanoates)

IT **135872-88-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as lipoxygenase and **phospholipase** A2 inhibitor)

IT **9001-84-7, Phospholipase** A2
RL: USES (Uses)
(inhibitors, substituted heterocycle- and indene alkanoates)

RN 9001-84-7 HCAPLUS
CN Phospholipase A2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L41 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1990:552250 HCAPLUS
DN 113:152250
TI Preparation of heterocyclic carboxamides as leukotriene antagonists
IN Brown, Frederick J.; Matassa, Victor G.
PA ICI Americas, Inc., USA
SO U.S., 47 pp. Cont.-in-part of U.S. Ser. No. 181,455, abandoned.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 4894386	A	19900116		US 1988-255914	19881011	<--
	ZA 8802483	A	19891227		ZA 1988-2483	19880408	<--
	DD 282683	A5	19900919		DD 1988-314744	19880414	<--
PRAI	US 1987-38853		19870415	<--			
	US 1987-103490		19871001	<--			
	US 1988-181455		19880414	<--			

OS CASREACT 113:152250; MARPAT 113:152250
GI For diagram(s), see printed CA Issue.
AB Title amides I [XYZ = C:CHN, NCH:C, C:NN, NN:C; R1 = H, alkyl and R2 = (unsatd.) alkyl, heteroalkyl, cycloalkyl, cycloalkylalkyl, Ph, phenylalkyl; or R1, R2 =H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl; or NR1R2 = heterocyclyl; M = (alkyl-substituted) alkylene, alkenylene; R9 = H, (substituted) alkyl; R10 = CO2H, CONHSO2R12, tetrazol-5-yl, COCH2SO2R12; R11 = H, alkoxy, alkyl, OH; R12 = (substituted) aryl, heteroaryl, aralkyl] were prepd. as leukotriene antagonists (no data). Thus, (indolylmethyl)benzoate deriv. II (R10 = CO2Me) was sapond. by LiOH in aq. MeOH-THF to give 92% II (R10 = CO2H), which was condensed with 2-MeC6H4SO2NH2 using a carbodiimide reagent to give 88% II (R10 = CONHSO2C6H4Me-2).

IT **119159-14-7P 119159-15-8P 119159-16-9P**
119159-17-0P 119159-18-1P 119160-06-4P
119160-09-7P 119160-17-7P 119160-57-5P
119160-58-6P 119160-59-7P 119160-60-0P
119160-61-1P 119160-87-1P 119188-69-1P
129525-06-0P 129525-07-1P 129525-08-2P
129525-20-8P 129525-21-9P 129525-22-0P
129525-23-1P 129525-24-2P 129525-25-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of leukotriene antagonists)

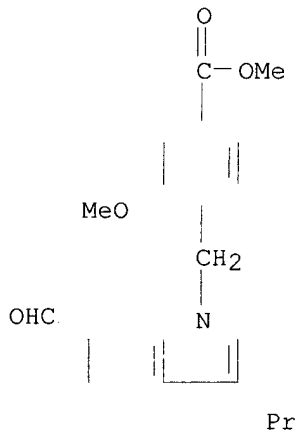
IT **119159-19-2P 119160-07-5P 119160-10-0P**

119160-18-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as leukotriene antagonist)

IT **119159-14-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of leukotriene antagonists)

RN 119159-14-7 HCAPLUS

CN Benzoic acid, 4-[(6-formyl-3-propyl-1H-indol-1-yl)methyl]-3-methoxy-, methyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2002 ACS

AN 1988:186571 HCAPLUS

DN 108:186571

TI Heterocyclic carboxamides, procedure for their preparation, and their use as leukotriene antagonists

IN Brown, Frederick Jeffrey; Yee, Ying Kwong

PA ICI Americas, Inc., USA

SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 242167	A2	19871021	EP 1987-303221	19870413 <--
	EP 242167	A3	19881012		
	EP 242167	B1	19911127		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ZA 8702313	A	19871125	ZA 1987-2313	19870330 <--
	DD 258984	A5	19880810	DD 1987-301317	19870331 <--
	AU 8771393	A1	19871022	AU 1987-71393	19870410 <--
	AU 602515	B2	19901018		
	DK 8701905	A	19871016	DK 1987-1905	19870413 <--
	AT 69812	E	19911215	AT 1987-303221	19870413 <--
	ES 2038172	T3	19930716	ES 1987-303221	19870413 <--
	FI 8701632	A	19871016	FI 1987-1632	19870414 <--
	NO 8701588	A	19871016	NO 1987-1588	19870414 <--
	SU 1597098	A3	19900930	SU 1987-4202446	19870414 <--
	PL 153341	B1	19910430	PL 1987-265151	19870414 <--
	CN 87103504	A	19871209	CN 1987-103504	19870415 <--
	HU 43819	A2	19871228	HU 1987-1655	19870415 <--

	HU 199791	B	19900328			
	JP 63008369	A2	19880114	JP 1987-91072	19870415	<--
	JP 07068211	B4	19950726			
	US 4898863	A	19900206	US 1987-38842	19870415	<--
	CA 1329933	A1	19940531	CA 1987-534855	19870415	<--
PRAI	GB 1986-9175		19860415	<--		
	GB 1986-24698		19861015	<--		
	EP 1987-303221		19870413	<--		

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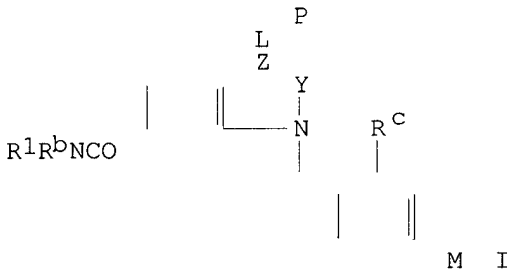


AB Carboxamides I [YZ< = CRa:C<, N:C<, N:C<, CHRaCH<; Ra = H, alkyl; Rb = H, Me; R1 = F (un)substituted alkyl, (un)substituted phenylalkyl, cycloalkyl or cycloalkylalkyl [cyclic group (un)substituted with alkyl]; L = alkylene with optional double or triple bond; P = polar group; Rc = H, alkoxy; M = acidic group selected from CO2H, CONHSO2R6 (R6 = alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl with halo, alkyl, alkoxy; or CF3 (un)substituted arom. or heteroarom. moiety] or their salts, useful as leukotriene antagonists for treating allergic or inflammatory diseases or endotoxic or traumatic shock conditions, were prepd. by 14 methods. N-[4-[6-(N-Cyclopentylmethylcarbamoyl)-3-[2-(pyrrolidinocarbonyl]ethyl]indol-1-ylmethyl]-3-methoxybenzoyl-2-methylbenzenesulfonamide (prepd. from the corresponding benzoic acid deriv.) was effective as a leukotriene antagonist at 2 mmol/kg in guinea pigs and showed no sign of overt toxicity following oral administration of 30 mmol/kg.

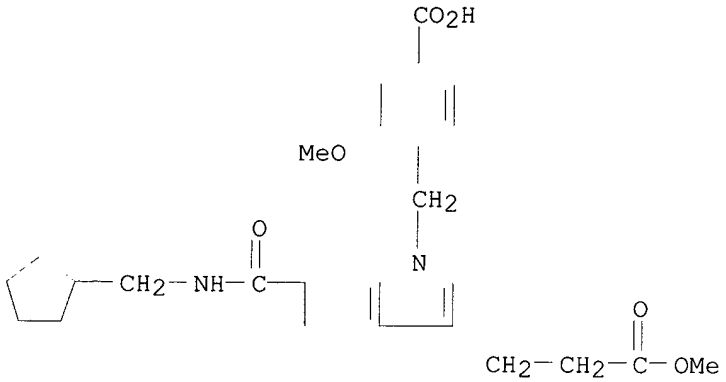
IT **114085-89-1P 114085-91-5P 114085-92-6P**
114085-93-7P 114086-16-7P 114086-20-3P
114086-21-4P 114086-23-6P 114086-24-7P
114086-25-8P 114086-26-9P 114086-27-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in synthesis of heterocyclic carboxamide leukotriene antagonists)

IT **114085-88-0P 114086-17-8P 114086-28-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as leukotriene antagonists)

IT **114085-89-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in synthesis of heterocyclic carboxamide leukotriene antagonists)

RN 114085-89-1 HCAPLUS

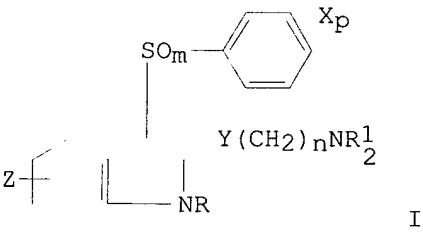
CN 1H-Indole-3-propanoic acid, 1-[(4-carboxy-2-methoxyphenyl)methyl]-6-[[(cyclopentylmethyl)amino]carbonyl]-, .alpha.-methyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:423236 HCAPLUS
DN 107:23236
TI Preparation and formulation of 1,2,3-trisubstituted indoles for treatment of inflammation
IN Greenhouse, Robert J.; Muchowski, Joseph M.
PA Syntex (U.S.A.), Inc., USA
SO U.S., 11 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4654360	A	19870331	US 1984-616346	19840601 <--

OS CASREACT 107:23236
GI



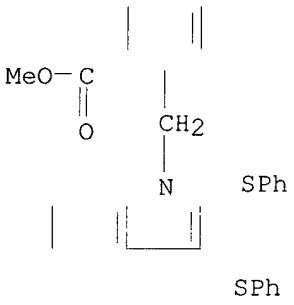
I

AB Title compds. I [R = C1-8 alkyl, (un)substituted PhCH2; R1 = H, C1-4 alkyl; X, Z = C1-4 alkyl, halo, HO, F3CO, HO2C, F3C, R2O, R2 = C1-4 alkyl, etc.; Y = S, NH, NR2; m = 0-2; n = 2-8; p = 0-5] and their salts were prepd. H2NCH2CH2SH-HCl in DMF was added to NaH, followed by 1-benzyl-2-chloro-3-(phenylsulfonyl)indole in DMF to give 1-benzyl-2-(aminoethylthio)-3-(phenylsulfonyl)indole. Inhibition of lipoxygenase activity was demonstrated.

IT **108726-72-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn. of)

IT **108698-87-9P 108726-74-5P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiinflammatory)

IT **108698-71-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiinflammatory agent)
IT **108698-72-2**
RL: RCT (Reactant)
(substitution reaction of, with aminoethanethiol)
IT **108726-72-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn. of)
RN 108726-72-3 HCAPLUS
CN Benzoic acid, 2-[[2,3-bis(phenylthio)-1H-indol-1-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1986:626346 HCAPLUS
DN 105:226346
TI Heterocyclic amides
IN Brown, Frederick Jeffrey; Bernstein, Peter Robert; Yee, Ying Kwong
PA ICI Americas, Inc., USA
SO Eur. Pat. Appl., 137 pp.
CODEN: EPXXDW
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 179619	A1	19860430	EP 1985-307498	19851017 <--
	EP 179619	B1	19900905		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	FI 8504024	A	19860420	FI 1985-4024	19851016 <--
	ZA 8507952	A	19860528	ZA 1985-7952	19851016 <--
	HU 38905	A2	19860728	HU 1985-4007	19851016 <--
	HU 194163	B	19880128		
	AU 8548814	A1	19860424	AU 1985-48814	19851017 <--
	AU 583062	B2	19890420		
	DD 253618	A5	19880127	DD 1985-281838	19851017 <--
	SU 1545940	A3	19900223	SU 1985-3970050	19851017 <--
	AT 56205	E	19900915	AT 1985-307498	19851017 <--
	DK 8504793	A	19860420	DK 1985-4793	19851018 <--
	DK 169541	B1	19941128		
	NO 8504163	A	19860421	NO 1985-4163	19851018 <--
	JP 61178963	A2	19860811	JP 1985-231457	19851018 <--
	JP 07045466	B4	19950517		
	ES 548011	A1	19870401	ES 1985-548011	19851018 <--
	IL 76756	A1	19890515	IL 1985-76756	19851018 <--

	CA 1273934	A1	19900911	CA 1985-493372	19851018 <--
	US 4997844	A	19910305	US 1985-788807	19851018 <--
	CN 85108623	A	19860730	CN 1985-108623	19851019 <--
	ES 554577	A1	19871201	ES 1986-554577	19860430 <--
	ES 554578	A1	19871201	ES 1986-554578	19860430 <--
	ES 554580	A1	19880216	ES 1986-554580	19860430 <--
	ES 554579	A1	19880616	ES 1986-554579	19860430 <--
	ES 554579	A5	19880714		
	SU 1595338	A3	19900923	SU 1987-4202434	19870424 <--
	US 5234942	A	19930810	US 1990-628787	19901217 <--
PRAI	GB 1984-26474		19841019 <--		
	GB 1985-7305		19850321 <--		
	GB 1985-7861		19850326 <--		
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	EP 1985-307498		19851017 <--		
	US 1985-788807		19851018 <--		

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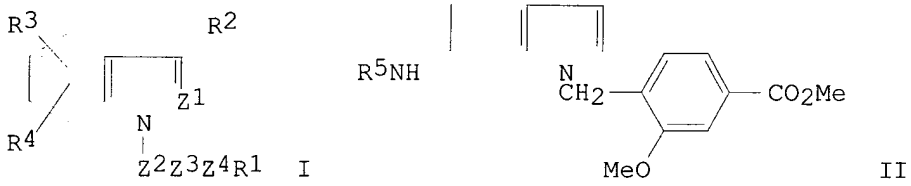


AB Title compds. I [Z1 = CH, N; Z2 = alkylene, alkenylene; Z3 = bond, O, S, phenylene, etc.; Z4 = CH2, CH:CH, bond; R1 = CO2H, 5-tetrazolyl , N-(organosulfonyl)carbamoyl, etc.; R2 = H, Me, halo, alkanoyl, etc.; R3 = H, halo, alkyl, alkoxy; R4 = acylamino, esterified NHCO2H, substituted ureido, H2NCO, etc.] were prepd. for treatment of allergic and inflammatory diseases. Indolamine II (R5 = H) was treated with hexanoyl chloride and Et3N to give II (R5 = hexanoyl). Selected I showed leukotriene antagonism in guinea-pigs at 5-50 mg orally. Capsules were prepd. contg. I 10, lactose 488.5, and Mg stearate 1.5 mg.

IT **104447-68-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of)

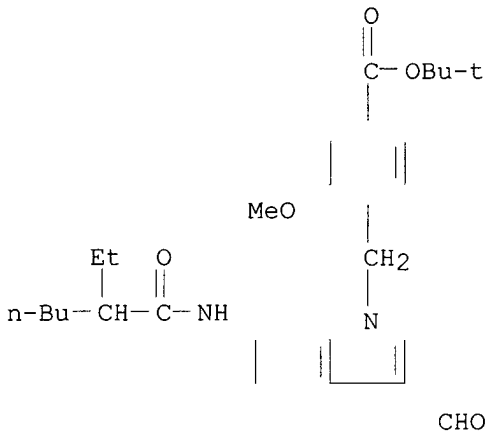
IT **104435-89-4P 104435-95-2P 104436-15-9P**
104436-16-0P 104436-41-1P 104436-42-2P
104436-43-3P 104436-44-4P 104436-47-7P
104436-48-8P 104436-97-7P 104436-99-9P
104446-89-1P 104446-91-5P 104446-94-8P
104447-01-0P 104447-24-7P 104447-27-0P
104447-61-2P 104447-67-8P 104447-69-0P
104447-70-3P 104447-71-4P 104448-09-1P
104448-12-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as a drug)

IT **104435-88-3 104447-70-3 104448-09-1**
RL: RCT (Reactant)
(reaction of)

IT **104447-68-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of)

RN 104447-68-9 HCAPLUS

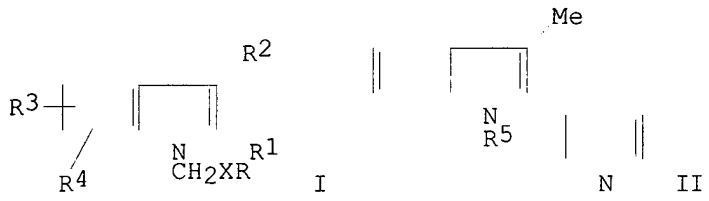
CN Benzoic acid, 4-[[6-[(2-ethyl-1-oxohexyl)amino]-3-formyl-1H-indol-1-yl]methyl]-3-methoxy-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1985:62093 HCAPLUS
DN 102:62093
TI N-Substituted-2-pyridylindoles
IN Renfroe, Harris B.
PA Ciba-Geigy Corp. , USA
SO U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 323,018, abandoned.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4478842	A	19841023	US 1982-437420	19821101 <--
	US 4460777	A	19840717	US 1982-419383	19820917 <--
	GB 2111050	A1	19830629	GB 1982-32457	19821112 <--
	GB 2111050	B2	19850911		
	FI 8203938	A	19830520	FI 1982-3938	19821117 <--
	FI 75344	B	19880229		
	FI 75344	C	19880609		
	DD 204924	A5	19831214	DD 1982-244959	19821117 <--
	ES 517439	A1	19841201	ES 1982-517439	19821117 <--
	CA 1197249	A1	19851126	CA 1982-415716	19821117 <--
	IL 67284	A1	19860331	IL 1982-67284	19821117 <--
	DK 8205141	A	19830520	DK 1982-5141	19821118 <--
	DK 169104	B1	19940815		
	NO 8203869	A	19830520	NO 1982-3869	19821118 <--
	NO 159929	B	19881114		
	NO 159929	C	19890222		
	AU 8290675	A1	19830526	AU 1982-90675	19821118 <--
	AU 564233	B2	19870806		
	ZA 8208505	A	19830928	ZA 1982-8505	19821118 <--
	HU 30607	O	19840328	HU 1982-3704	19821118 <--
	HU 190425	B	19860929		
	JP 58092677	A2	19830602	JP 1982-203514	19821119 <--
	JP 02009031	B4	19900228		
	ES 530126	A1	19851116	ES 1984-530126	19840228 <--
	ES 530128	A1	19851201	ES 1984-530128	19840228 <--
	ES 530127	A1	19860616	ES 1984-530127	19840228 <--
PRAI	US 1981-323018		19811119 <--		

OS CASREACT 102:62093
GI



AB Thromboxane synthetase inhibiting title compds. I [R = CO2H, H2NCO, HCO, acyl, 5-tetrazolyl; R1 = (un)substituted pyridyl; R2 = H, alkyl; R3, R4 = H, alkyl, halo, CF3, OH, alkoxy, CO2H, etc.; R3R4 = alkylenedioxy; X = C1-C12 alkylene, optionally contg. S, O, or phenylene] were prepd. Thus, pyridylindole II (R5 = H) was alkylated with Br(CH2)7CO2Me to give II [R5 = (CH2)7CO2Me], which was hydrolyzed to form II [R5 = (CH2)7CO2H] (III). At 30 mg/kg orally in rats, III prolonged bleeding time. III protected mice against arachidonic acid induced pulmonary obstruction at 100 mg/kg orally.

IT **87627-79-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)

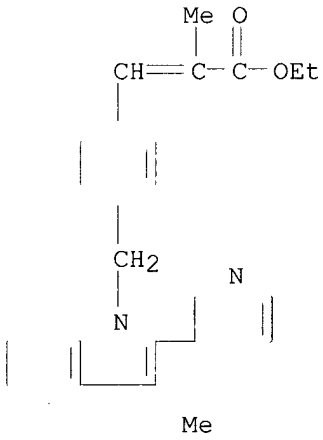
IT **87627-37-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and thromboxane synthetase inhibition by)

IT **87627-70-1P 94454-47-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **87627-79-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)

RN 87627-79-0 HCAPLUS

CN 2-Propenoic acid, 2-methyl-3-[4-[[3-methyl-2-(3-pyridinyl)-1H-indol-1-yl]methyl]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



L41 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2002 ACS

AN 1983:575589 HCAPLUS

DN 99:175589

TI N-Substituted 2-pyridylindoles, their pharmaceutical compositions, and their therapeutical use

IN Renfroe, Harris Burt

PA Ciba-Geigy A.-G. , Switz.

SO Eur. Pat. Appl., 77 pp.

CODEN: EPXXDW
DT **Patent**
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	EP 80154	A2	19830601		EP 1982-110582	19821116	<--
	EP 80154	A3	19830928				
	EP 80154	B1	19850828				
	R: AT, BE, CH, DE, FR, IT, LI, LU, NL, SE						
	US 4460777	A	19840717		US 1982-419383	19820917	<--
	GB 2111050	A1	19830629		GB 1982-32457	19821112	<--
	GB 2111050	B2	19850911				
	AT 15196	E	19850915		AT 1982-110582	19821116	<--
	FI 8203938	A	19830520		FI 1982-3938	19821117	<--
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	FI 75344	C	19880609				
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	ES 517439	A1	19841201		ES 1982-517439	19821117	<--
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	NO 8203869	A	19830520		NO 1982-3869	19821118	<--
	NO 159929	B	19881114				
	NO 159929	C	19890222				
	AU 8290675	A1	19830526		AU 1982-90675	19821118	<--
	AU 564233	B2	19870806				
	ZA 8208505	A	19830928		ZA 1982-8505	19821118	<--
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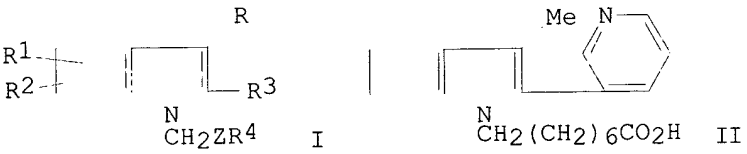
OS CASREACT 99:175589
GI



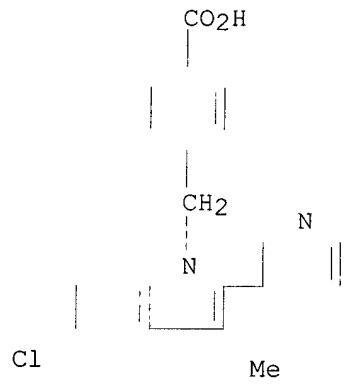
AB I [R = H, or lower alkyl; R1, R2 = H, alkyl, halo, CF3, etc.; R3 = (un)substituted pyridyl; R4 = CO2H or deriv.; Z = C1-12 alkylene, alkenylene, etc.] were prepd. and shown to inhibit thromboxane synthetase. Thus, 3-methyl-2-(3-pyridyl)indole was treated with Me3COK and Br(CH2)7CO2Me and the product hydrolyzed to give II.

IT **87627-70-1P 87627-79-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **87627-37-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, and inhibition of thromboxane synthetase by)

IT **87627-70-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 87627-70-1 HCAPLUS
CN Benzoic acid, 4-[[5-chloro-3-methyl-2-(3-pyridinyl)-1H-indol-1-yl]methyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

L41 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2002 ACS
AN 1982:615993 HCAPLUS
DN 97:215993
TI Indole thromboxane synthetase inhibitors and their pharmaceutical compositions
IN Cross, Peter Edward; Dickinson, Roger Peter
PA Pfizer Ltd., UK; Pfizer Corp.
SO Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 54417	A1	19820623	EP 1981-305836	19811210 <--
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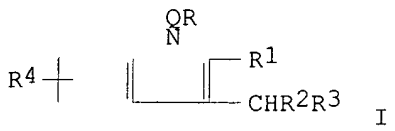
	FI 8104003	A	19820616	FI 1981-4003	19811214 <--
	NO 8104264	A	19820616	NO 1981-4264	19811214 <--
	AU 8178488	A1	19820624	AU 1981-78488	19811214 <--
	AU 525296	B2	19821028		
	ZA 8108665	A	19821027	ZA 1981-8665	19811214 <--
	JP 57181082	A2	19821108	JP 1981-201438	19811214 <--
	CA 1143737	A1	19830329	CA 1981-392225	19811214 <--
	DD 202290	A5	19830907	DD 1981-235742	19811214 <--
	ES 507960	A1	19831001	ES 1981-507960	19811214 <--
	HU 29693	O	19840228	HU 1981-3762	19811214 <--
	CS 228527	P	19840514	CS 1981-9343	19811215 <--
	PL 133634	B1	19850629	PL 1981-234253	19811215 <--
PRAI	GB 1980-40081		19801215 <--		

GI



I

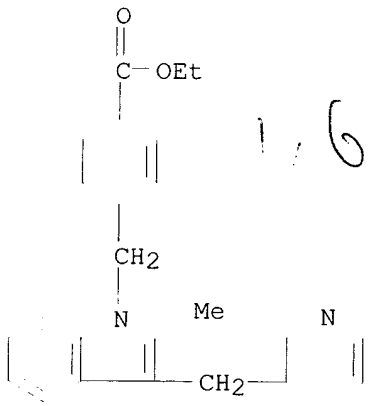
AB Thromboxane synthetase-inhibiting indoles [I; R = CO2H, alkoxycarbonyl, CONH2, CN or 5-tetrazolyl; R1 = H, alkyl, cycloalkyl or Ph; R2 = H or alkyl; R3 = 3- or 4-pyridyl; R4 = H, alkyl, alkoxy or halo; Q = (CH2)1-3, CH2CHMe or CH2C6H4] and their salts were prepd. Thus, treatment of 2-methyl-3-(3-pyridylmethyl)indole with acrylonitrile followed by hydrolysis gave I (R = CO2H, R1 = Me, R2 = R4 = H, R3 = 3-pyridyl) which, at 1.0 mg/kg i.v. in rabbits, gave 97 and 95%, resp., inhibition of thromboxane synthetase after 2 and 75 min.

IT **83795-18-0P 83795-19-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **83795-18-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 83795-18-0 HCAPLUS

CN Benzoic acid, 4-[[2-methyl-3-(3-pyridinylmethyl)-1H-indol-1-yl]methyl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

=> fil reg
FILE 'REGISTRY' ENTERED AT 15:01:09 ON 22 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 21 APR 2002 HIGHEST RN 406458-32-0
DICTIONARY FILE UPDATES: 21 APR 2002 HIGHEST RN 406458-32-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s l43 and l26-l30
L46 1 L43 AND (L26 OR L27 OR L28 OR L29 OR L30)

=> d ide can

L46 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **9001-84-7** REGISTRY
CN **Phospholipase A2 (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Acanthoxin A1
CN Agelotoxin
CN Ammodytoxin C
CN **Calcium-dependent phospholipase A2**
CN Conodipine-M
CN E.C. 3.1.1.4
CN Lecitase
CN Lecitase 10L
CN Lecithinase A
CN Nigroxin C1
CN Nigroxin C2
CN Nigroxin C3
CN Phosphatidase
CN Phosphatide acyl-hydrolase
CN Phosphatidolipase
CN **Phospholipase A**
CN **Phospholipase III**
CN Phospholipin
CN PLA2
CN Superbin
CN Superbin a
CN Superbin b
CN Superbin c
CN Superbin d
CN Superbin I
CN Superbin II
DR 195159-59-2, 195159-60-5
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
CA, CABA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM,
EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NAPRALERT, PROMT, RTECS*,
TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
11525 REFERENCES IN FILE CA (1967 TO DATE)
106 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
11543 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:268112

REFERENCE 2: 136:261776

REFERENCE 3: 136:261736

REFERENCE 4: 136:261218

REFERENCE 5: 136:261094

REFERENCE 6: 136:261031

REFERENCE 7: 136:260940

REFERENCE 8: 136:259094

REFERENCE 9: 136:258569

REFERENCE 10: 136:258482

=> s l43 not l46
L47 142 L43 NOT L46

=> d reg tot

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25	RN	**220690-16-4**	REGISTRY
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38	RN	**192585-79-8**	REGISTRY
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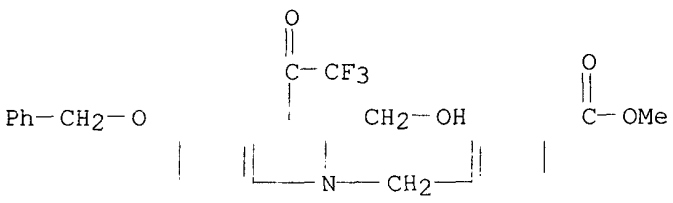
137 RN **94454-47-4** REGISTRY
138 RN **87627-79-0** REGISTRY
139 RN **87627-70-1** REGISTRY
140 RN **87627-37-0** REGISTRY
141 RN **83795-19-1** REGISTRY
142 RN **83795-18-0** REGISTRY

=> d ide can 1 21 27 30 31 33 36 38 46 50 52 54 61 62 71 72 90 105 107 110 124 137 138 141

L47 ANSWER 1 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **241494-20-2** REGISTRY
CN Benzoic acid, 4-[[2-(hydroxymethyl)-5-(phenylmethoxy)-3-(trifluoroacetyl)-1H-indol-1-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H22 F3 N O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:199618

L47 ANSWER 21 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **220690-20-0** REGISTRY
CN 1H-Indole-6-carboxylic acid, 2-[[(4-methoxybenzoyl)methylamino]methyl]-3-[2-(methoxycarbonyl)-1-cyclopenten-1-yl]-1-[[4-(methoxycarbonyl)phenyl]methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C35 H34 N2 O8
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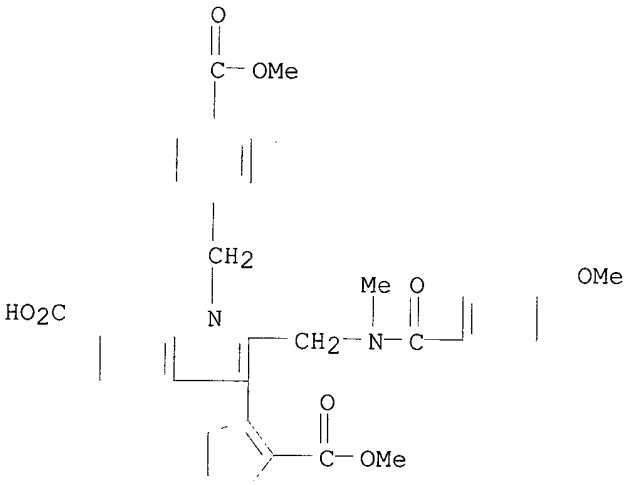
LC STN Files: CA, CAPLUS



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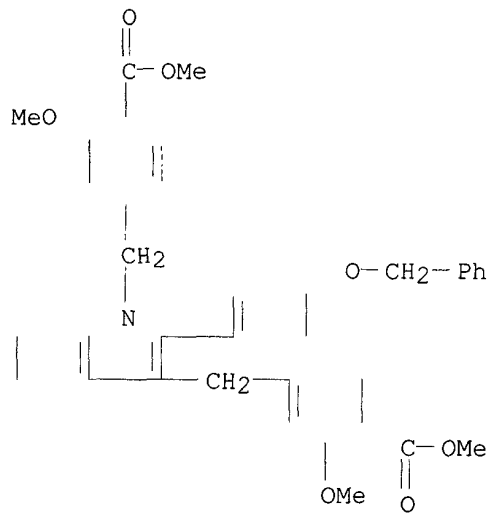
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:182357

L47 ANSWER 27 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **215584-38-6** REGISTRY
CN Benzoic acid, 4,4'-[[2-[4-(phenylmethoxy)phenyl]-1H-indole-1,3-diyl]bis(methylene)]bis[2-methoxy-, dimethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C41 H37 N O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

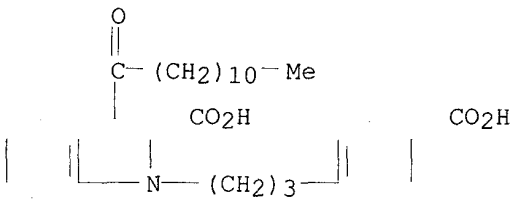


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:343412

L47 ANSWER 30 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **205106-44-1** REGISTRY
CN 1H-Indole-2-carboxylic acid, 1-[3-(4-carboxyphenyl)propyl]-3-(1-oxododecyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H39 N O5
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

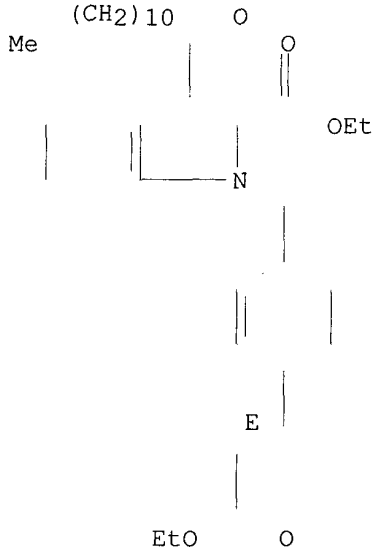
REFERENCE 1: 136:85739

REFERENCE 2: 128:257331

L47 ANSWER 31 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **203111-24-4** REGISTRY
CN 1H-Indole-2-carboxylic acid, 1-[[4-(3-ethoxy-3-oxo-1-

propenyl)phenyl]methyl]-3-(1-oxododecyl)-, ethyl ester, (E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H45 N O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Double bond geometry as shown.

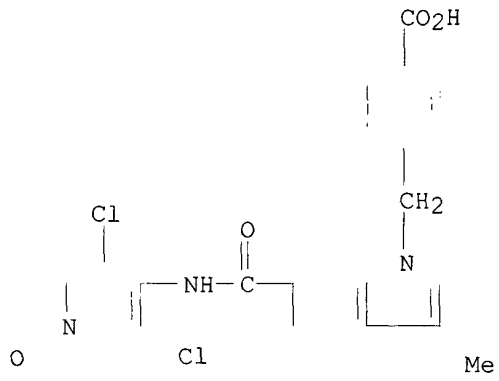


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:167350

L47 ANSWER 33 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **201286-15-9** REGISTRY
CN Benzoic acid, 4-[[6-[[(3,5-dichloro-1-oxido-4-pyridinyl)amino]carbonyl]-3-methyl-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H17 Cl2 N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



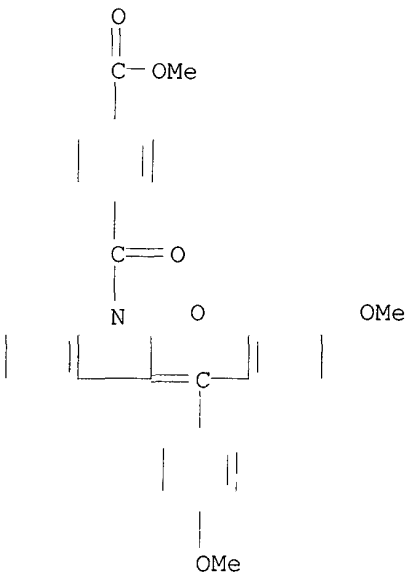
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:110138

REFERENCE 2: 128:102087

L47 ANSWER 36 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **193620-97-2** REGISTRY
CN Benzoic acid, 4-[[3-[bis(4-methoxyphenyl)methylene]-2,3-dihydro-2-oxo-1H-indol-1-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C32 H25 N O6
SR CA
LC STN Files: CA, CAPLUS

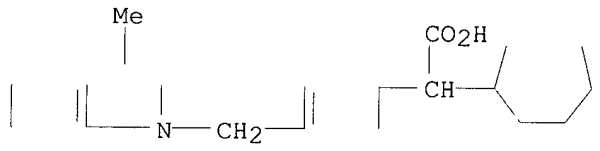


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:190643

L47 ANSWER 38 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **192585-79-8** REGISTRY
CN Cycloheptaneacetic acid, .alpha.-[4-[(3-methyl-1H-indol-1-yl)methyl]phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H29 N O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

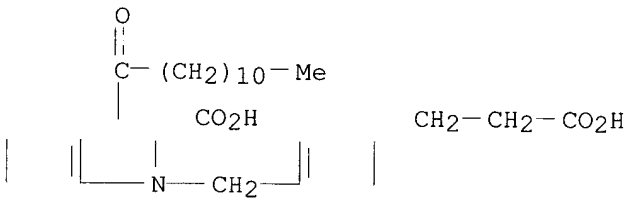


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:121734

L47 ANSWER 46 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **192182-39-1** REGISTRY
CN 1H-Indole-2-carboxylic acid, 1-[[4-(2-carboxyethyl)phenyl]methyl]-3-(1-oxododecyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H39 N O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



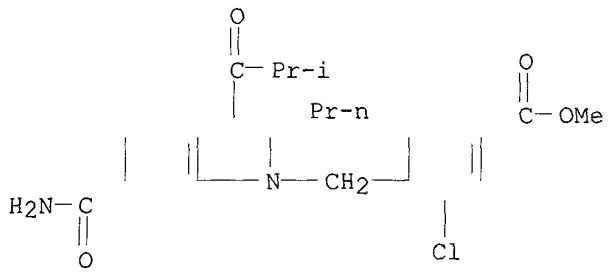
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:167350

REFERENCE 2: 127:90133

L47 ANSWER 50 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **184150-66-1** REGISTRY
CN Benzoic acid, 4-[[6-(aminocarbonyl)-3-(2-methyl-1-oxopropyl)-2-propyl-1H-indol-1-yl]methyl]-3-chloro-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H27 Cl N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

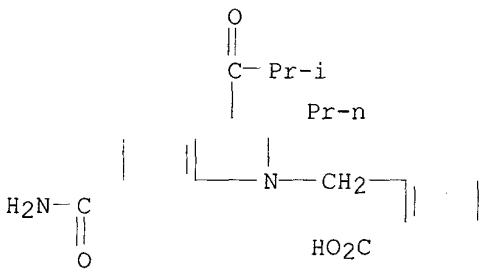
REFERENCE 1: 136:247492

REFERENCE 2: 129:45274

REFERENCE 3: 128:275074

REFERENCE 4: 126:18786

L47 ANSWER 52 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **184148-89-8** REGISTRY
CN Benzoic acid, 2-[[6-(aminocarbonyl)-3-(2-methyl-1-oxopropyl)-2-propyl-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H26 N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

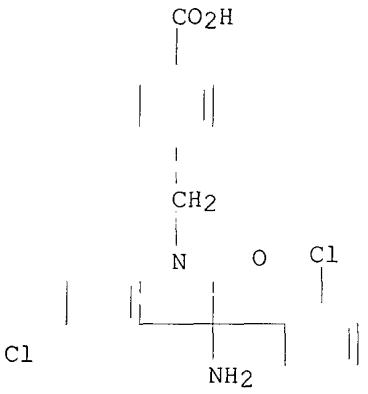
REFERENCE 1: 136:247492

REFERENCE 2: 129:45274

REFERENCE 3: 128:275074

REFERENCE 4: 126:18786

L47 ANSWER 54 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **169040-74-8** REGISTRY
CN Benzoic acid, 4-[[3-amino-5-chloro-3-(2-chlorophenyl)-2,3-dihydro-2-oxo-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H16 Cl2 N2 O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

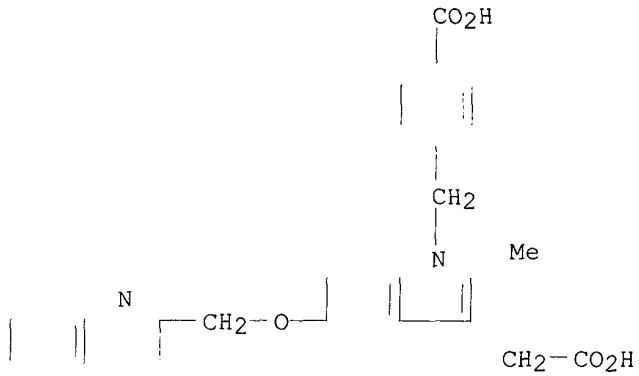


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:256516

L47 ANSWER 61 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **135872-88-7** REGISTRY
CN 1H-Indole-3-acetic acid, 1-[(4-carboxyphenyl)methyl]-2-methyl-5-(2-quinolinylmethoxy)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H24 N2 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

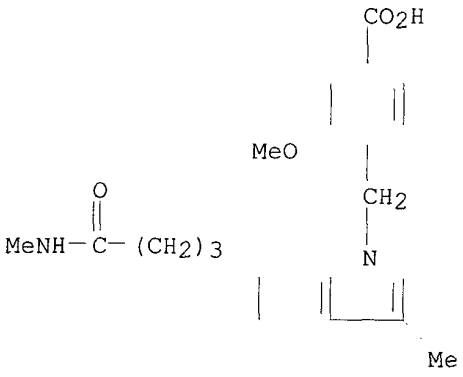
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:8801

REFERENCE 2: 120:298483

REFERENCE 3: 115:135935

L47 ANSWER 62 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **129525-25-3** REGISTRY
CN Benzoic acid, 3-methoxy-4-[[3-methyl-6-[4-(methylamino)-4-oxobutyl]-1H-indol-1-yl]methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H26 N2 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

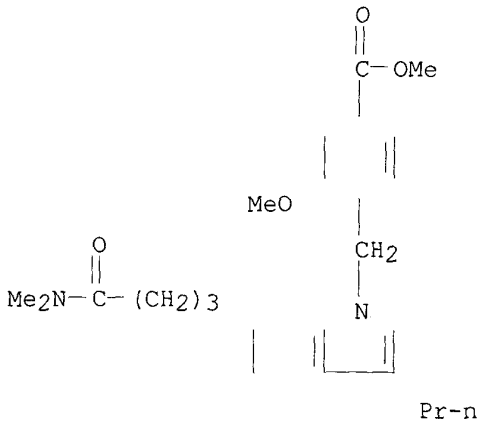


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 113:152250

L47 ANSWER 71 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **119188-69-1** REGISTRY
CN Benzoic acid, 4-[[6-[4-(dimethylamino)-4-oxobutyl]-3-propyl-1H-indol-1-yl]methyl]-3-methoxy-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H34 N2 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



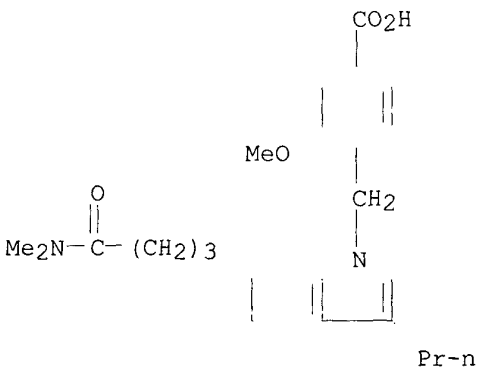
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 113:152250

REFERENCE 2: 110:154147

L47 ANSWER 72 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **119160-87-1** REGISTRY
CN Benzoic acid, 4-[[6-[4-(dimethylamino)-4-oxobutyl]-3-propyl-1H-indol-1-yl]methyl]-3-methoxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H32 N2 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



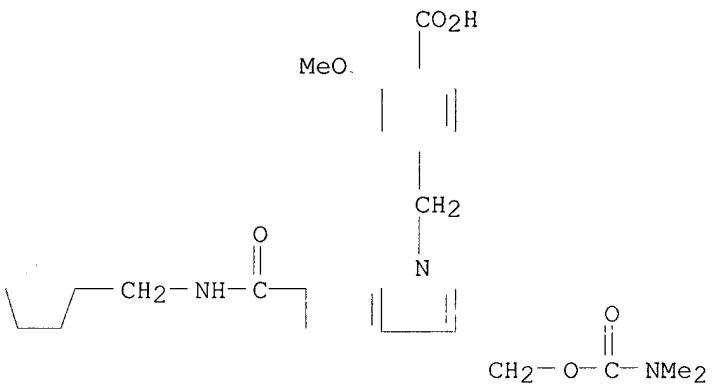
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 113:152250

REFERENCE 2: 110:154147

L47 ANSWER 90 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **114086-28-1** REGISTRY
CN Benzoic acid, 4-[[6-[[(cyclopentylmethyl)amino]carbonyl]-3-[[[(dimethylamino)carbonyl]oxy]methyl]-1H-indol-1-yl]methyl]-2-methoxy- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C28 H33 N3 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

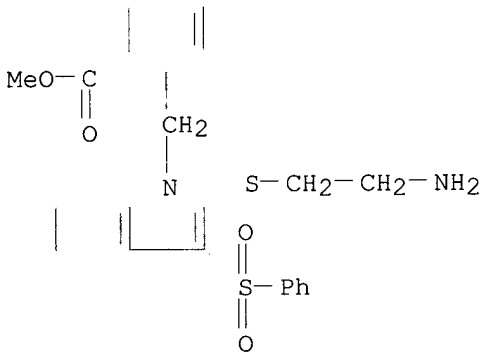


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 108:186571

L47 ANSWER 105 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **108726-74-5** REGISTRY
CN Benzoic acid, 2-[[2-[(2-aminoethyl)thio]-3-(phenylsulfonyl)-1H-indol-1-yl]methyl]-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)
MF C25 H24 N2 O4 S2 . x Cl H
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (108698-71-1)

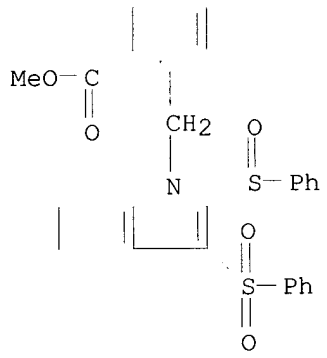


● x HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 107:23236

L47 ANSWER 107 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **108698-87-9** REGISTRY
CN Benzoic acid, 2-[[2-(phenylsulfinyl)-3-(phenylsulfonyl)-1H-indol-1-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)
MF C29 H23 N O5 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



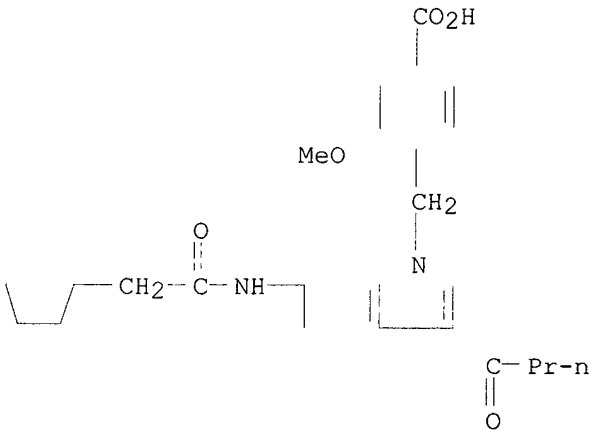
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 107:23236

L47 ANSWER 110 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **104448-12-6** REGISTRY
CN Benzoic acid, 4-[[6-[(cyclopentylacetyl)amino]-3-(1-oxobutyl)-1H-indol-1-yl]methyl]-3-methoxy- (9CI) (CA INDEX NAME)

FS 3D CONCORD
MF C28 H32 N2 O5
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)



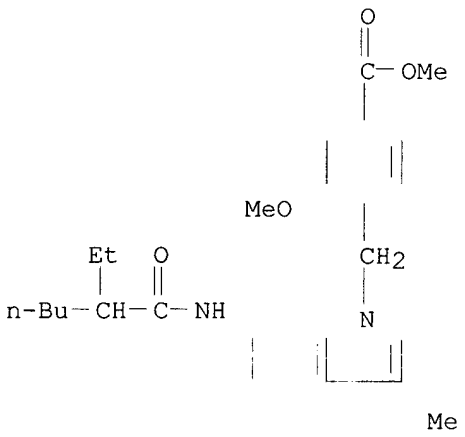
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 117:90198

REFERENCE 2: 105:226346

L47 ANSWER 124 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **104436-99-9** REGISTRY
CN Benzoic acid, 4-[[6-[(2-ethyl-1-oxohexyl)amino]-3-methyl-1H-indol-1-yl]methyl]-3-methoxy-, methyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H34 N2 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

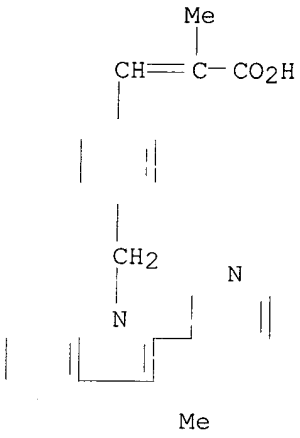


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 105:226346

L47 ANSWER 137 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **94454-47-4** REGISTRY
CN 2-Propenoic acid, 2-methyl-3-[4-[[3-methyl-2-(3-pyridinyl)-1H-indol-1-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H22 N2 O2
LC STN Files: CA, CAPLUS, USPATFULL

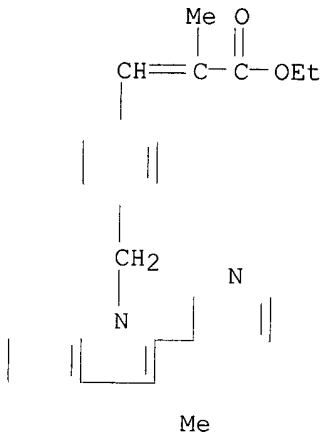


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 102:62093

L47 ANSWER 138 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **87627-79-0** REGISTRY
CN 2-Propenoic acid, 2-methyl-3-[4-[[3-methyl-2-(3-pyridinyl)-1H-indol-1-yl]methyl]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H26 N2 O2
LC STN Files: CA, CAPLUS, USPATFULL



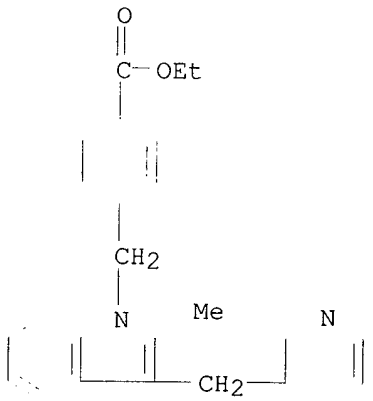
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 102:62093

REFERENCE 2: 99:175589

L47 ANSWER 141 OF 142 REGISTRY COPYRIGHT 2002 ACS
RN **83795-19-1** REGISTRY
CN Benzoic acid, 4-[[2-methyl-3-(3-pyridinylmethyl)-1H-indol-1-yl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H24 N2 O2
CI COM
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:215993

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     (FILE 'HOME' ENTERED AT 15:15:16 ON 22 APR 2002)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 15:15:28 ON 22 APR 2002
               E 65:3843/OREF
L1            3 S E8


=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:16:43 ON 22 APR 2002
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FILE COVERS 1907 - 22 Apr 2002  VOL 136 ISS 17
FILE LAST UPDATED: 21 Apr 2002  (20020421/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
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information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d all l1 tot

L1   ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2002 ACS
AN   1966:420747  HCAPLUS
DN   65:20747
OREF 65:3843e-h,3844a-c
TI   Isomeric 7-(diphenylmethyl)-7-hydroxy-2,3-norbornanedicarboxylic acid
     .gamma.-lactones
IN   Poos, George I.
PA   McNeil Laboratories, Inc.
SO   11 pp.; Continuation-in-part of U.S. 3,203,983 (CA 64, 657d)
DT   Patent
LA   Unavailable
NCL  260343300
CC   37 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1
     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
     ---------------  ----  --------      ---------------  --------
PI   US 3250789             19660510      US               19640521
GI   For diagram(s), see printed CA Issue.
AB   A fulvene and a maleimide by a Diels-Alder reaction give a
     5-norbornenedicarboximide.  Thus, a soln. of 2.3 parts 6,6-diphenylfulvene
     and 1.11 parts N-methylmaleimide in 10 parts by vol. C6H6 after 4 days at
```

25.degree. gave endo-I (Y = diphenylmethylene, R = Me) (Ia), m. 173-4.degree.. A soln. of 5 parts BzOOH in CHCl3 added to a soln. of 12.35 parts Ia in 100 parts by vol. CHCl3 after 36 hrs. at 25.degree. gave the corresponding epoxide, m. 181.5-2.5.degree.. iso-; mer, Y, R, m.p.; exo, Ph2CH:, Me, 154-7.degree.; endo, Ph2CH:, Et, 125-6.degree.; endo, Ph2CH:, PhCH2CH2, 174-6.degree.; endo, Ph2CH2, Me, 206.5-9.0.degree.; --, Me2CH:, H, 176-80.degree.; --, Me2CH:, Me, 142-3.degree.; endo, bis(p-chlorophenyl)methylene, H, 205-7.degree.; endo, bis(p-chlorophenyl)methylene, Me, 132-6.degree.; --, phenyl-2-pyridylmethylene, H, 217-18.degree.; --,phenyl-2-pyridylmethylene, Me, 169-70.degree.; endo, bis(m-trifluoromethylphenyl)methylene, H, 180-3.degree.; endo, bis(m-trifluoromethylphenyl)methylene, Me, 135-7.degree. --, bis(o-methylphenyl)methylene, H, 185-8.5.degree.; endo, bis(o-methylphenyl)methylene, Me, 161-2.degree.; --, 1-phenylethylidene, H, 159-61.degree.; endo, 1-phenylethylidene, Me, 170-2.degree.; endo, Ph2CH:, carbamoyl, 200-10.degree.; endo, Ph2CH:, .beta.-hydroxyethyl, 171-2.degree.; endo, diphenylmethyl-.gamma.-epoxy, Me, 181.5-2.5.degree.. Similarly prepd. I were: exo-7-(di-phenylmethylene)-5,6-epoxy-N-methyl-2,3-norbornenedicarboximide, m. 179.5-81.5.degree. and the compds. listed in the 1st table. over Pd on C gave 1.63 parts endo-7-(diphenylmethyl)-7-hydroxy-N-methyl-2,3-norbornanedicarboximide (Ib), m. 276-80.degree.. Ib (9.8 parts) refluxed 6 hrs. in a soln. of 50 parts KOH in 250 parts H2O and 250 parts by vol. EtOH gave 7-(diphenylmethyl)-7-hydroxy-2,3-norbornanedicarboxylic acid (isomer A), m. 140-5.degree. and (isomer B), m. 258-60.degree.. Isomer A (90 parts) treated with 0.5 part by vol. AcCl 2 hrs. at 60.degree. gave the corresponding .gamma.-lactone, m. 191-2.5.degree.. Similarly, isomer B overnight at 60.degree. gave a .gamma.-lactone, m. 253-9.degree.. Redn. of I gave the corresponding 4,7-methanoisoindoline (II). Thus, 1.75 parts Ia in ether added to 9.5 parts LiAlH4 in ether gave, after 2.5 hrs. reflux, endo-II (Y = diphenylmethylene, R = Me), m. 74-7.degree.. Similarly prepd. II are tabulated in the 2nd table. iso-, deriv. and/or; mer, Y, R, m.p.; endo, Ph2CH:, Me, fumarate, 203.5-5.5.degree.;, (decompn.); exo, Ph2CH:, Me, fumarate, 176-8.degree.; endo, Ph2CH:, Et, 90.5-2.5.degree.; endo, Ph2CH:, PhCH2CH2, maleate, 178-9.degree.; endo, Ph2CH:*, Me, fumarate. 191-2.degree.; endo, Ph2CH2*, Me, fumarate, 237-8.degree.; --, Me2CH:, Me, fumarate, 144-9.degree.; endo, bis(p-chlorophenyl)methylene, Me, maleate, 160-1.degree.; endo, phenyl-2-pyridylmethylene, Me, fumarate, 175-6.degree.; --, bis(m-trifluoromethylphenyl)-, Me, maleate, 143-5.5.degree.;, methylene,; endo, bis(o-methylphenyl)methylene, Me, maleate, 140.5-42.degree.; --, 1-phenylethylidene, Me, fumarate, 164-5.degree.; endo, Ph2CH: .beta.-hydroxy-, fumarate, 176-9.degree.; ethyl,; endo, Ph2CH:, H, maleate, 186.5-90.degree.; endo, Ph2CH:, Me, 151-2.degree.; *, 5,6-positions reduced.

L1 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 1966:420746 HCAPLUS
DN 65:20746
OREF 65:**3843e**
TI .alpha.-(1-Benzyl-3-indolyl)alkane carboxylic acids
IN Sarett, Lewis H.; Shen, Tsung-Ying
PA Merck & Co. Inc.
SO 19 pp.
DT Patent
LA Unavailable
NCL 260211000
CC 37 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3242163		19660322	US	19610313
	NL 6513089			NL	

AB Identical with U.S. 3,242,193 (preceding abstr.), except that the claims

for R4 are limited to CN, CO2H, and carbalkoxy.

L1 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 1966:420745 HCAPLUS
DN 65:20745
OREF 65:**3840e-h,3841a-h,3842a-h,3843a-e**
TI .alpha.-(1-Benzyl-3-indolyl)alkanecarboxylic acids
IN Sarett, Lewis H.; Shen, Tsung-Ying
PA Merck & Co. Inc.
SO 20 pp.
DT Patent
LA Unavailable
NCL 260319000
CC 37 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3242193		19660322	US	19641021

GI For diagram(s), see printed CA Issue.
AB Division of U.S. 3,196,162 (CA 63, 16308a). Cf. following abstr. The reaction in alc. HCl solns. of R4C6H4NHNH2 and R2COCH2CHR3CO2Y give II. The title compds. (I) are prepd. by treatment of II with NaH or other metalating agents, followed by R5bC6H5-bCHR1X. Addn. of 100 g. p-MeC6H4SH in 250 ml. (MeOCH2)2 during 2 hrs. to 41.5 g. 50% NaH dispersion in mineral oil in (MeOCH2)2 at -5 to 0.degree., followed by addn. of 20 ml. Me3COH and stirring 15 min. at 0.degree., then bubbling CHF2Cl through the mixt. 45 min. at -2 to 0.degree., and standing 14 hrs. gave 112.3 g. p-MeC6H4SCHF2 (III), b0.35 32-4.degree., n23D 1.5092. One mole p-MeC6H4OH was similarly converted to 18.5 g. p-MeC6H4OCHF2 (IV), m. 165-7.degree.. Treatment of 8.7 g. III with 8.9 g. (CH2CO)2NBr in 400 ml. CCl4 under irradiation by a 275-watt sun lamp 2 hrs. gave 7.0 g. p-CHF2SC6H4CH2Br (IVa), b0.3 74.degree., n22D 1.5622. IV (14.6 g.) and 16.4 g. (CH2CO)2NBr in 800 ml. CCl4 gave 18.5 g. p-HF2COC6H4CH2Br (V), b0.2 50-52.degree., n23D 1.5170. Treatment of 59.7 g. p-MeC6H4SO2NMe2 with 53.4 g. (CH2CO)2NBr in 500 ml. refluxing CCl4 2.5 hrs. gave p-(Me2N SO2)C6H4CH2Br (VI), m. 85-108.degree. (Skellysolve B). MeSPh (120 g.) and 69 g. MeOCH2Cl in 600 ml. HOAc kept at 78-80.degree. for 2 days, evapd., and distd. gave 68 g. p-MeSC6H4CH2Cl (VII), b1 99.degree.. MeSH (24 g.) was bubbled into 350 ml. EtOH containing 32.5 g. 86.5% KOH, 1.2 ml. H2O was added, followed by 70.3 g. p-ClC6H4CHO in 150 ml. EtOH, and the mixt. was refluxed 3 hrs. with slow introduction of MeSH, then poured into 500 ml. H2O, and extd. with ClCH2CH2Cl, giving p-MeSC6H4CHO, redn. of which by Al(OCHMe2)3 in Me2CHOH, followed by treatment with SOCl2, also gave VII. Action of 82 ml. MeOCH2Cl on 177 g EtSPh in 770 ml. HOAc at 75.degree. 48 hrs. gave p-EtSC6H4CH2Cl (VII), b0.025-0.04 92-102.degree.. Similar treatment of 100 ml. Ph2S with 36.3 ml. MeOCH2Cl in 340 ml. HOAc gave 32 g. of a distillate, b0.005 85-145.degree., which contained 39% p-PhSC6H4CH2Cl (IX). A soln. of 25 g. p-H2NC6H4CH2OH in 200 ml. H2O and 80 ml. HCl at 0-5.degree. was treated with 15.5 g. NaNO2 in 40 ml. H2O and neutralized with KOAc. The cold, neutral soln. was filtered into a soln. of 97.6 g. EtOCS2K in 1000 ml. H2O at 75-80.degree., and the mixt. was heated 1 hr. on a steam bath, cooled, and extd. with 3 250-ml. portions Et2O. The exts. were washed thrice with 250 ml. portions H2O, dried, and evapd. To the residual red oil was added 33 g. KOH in 300 ml. EtOH, the mixt. was refluxed 2 hrs. under N, 50.6 g. PhCH2Cl was added, and refluxing continued 3 hrs. to give p-PhCH2SC6H4CH3OH (XI), m. 75-81.degree. (4:35 C6H6-cyclohexane). Action of 100 ml. SOCl2 on 10.7 g. X at 0.degree. 1 hr. gave p-PhCH2SC6H4CH2Cl, m. 91-3.degree. (EtOH). To 7.92 g. Mg in 50 ml. Et2O was added 10 ml. of a soln. of 61 g. p-F3CC6H4Br in 60 ml. Et2O, followed by 2 ml. MeMgI soln. under N. After initiation of the reaction, 200 ml. Et2O and the rest of the p-F3CC6H4Br soln. were added during 1 hr. After refluxing 1.5 hrs., the soln. was cooled to 5.degree. and 81 g. PhNMeCHO was added over 20 min. After 2 hrs. in an ice bath and 18 hrs.

at room temp., the mixt. was treated with 200 ml. 5N H2SO4 with cooling, giving p-F3CC6H4CHO (XI), b12 64.degree., n22D 1.4633. Redn. of 20.9 g. XI with 2.5 g. NaBH4 in 100 ml. C6H6, and treatment with 14 g. SOCl2, gave p-F3CC6H4CH2Cl, b12 68.degree., n22D 1.4622. Mixing 53.3 g. p-H2NC6H4SH in 200 ml. EtOH and 60.2 g. p-ClC6H4CHO in 200 ml. EtOH gave, in 20 min., 97 g. p-ClC6H4CH:NC6H4SH-p (XII). Treatment of 58.2 g. XII with 11.52 g. NaH in 400 ml. Me2NCHO during 2 hrs., then addn. of 35 g. MeI in 100 ml. Me2NCHO during 1 hr., and diln. with 2l. H2O, gave p-ClC6H4CH:NC6H4SMe-p, 12 g. of which was reduced by 4.0 g. NaBH4 in 300 ml. MeOH to give p-ClC6H4CH2NHC6H4SMe-p (XIII). Nitrosation of XIII gave the N-nitroso deriv., redn. of 38 g. of which by Al amalgam in Me2CHOH gave p-ClC6H4N(NH2)C6H4SMe-p; hydrochloride (XIIIa) m. 140.5.degree. (EtOH). A soln. of 44 g. p-MeOC6H4NHNH2.HCl (XIV), 42 g. p-O2NC6H4CH2Cl, and 80 g. Et3N in 500 ml. EtOH was refluxed 6 hrs., and 70 ml. 3.2N HCl in EtOH was added, giving 14.4 g. p-MeOC6H4N(NH2)CH2C6H4NO2-p.HCl (XV), m. 147-50.degree.. Hydrogenation of 37 g. p-MeOC6H4NH2 and 50 g. 2,4-(MeO)2C6H3CHO in 250 ml. EtOH on Ni at 40 psi. gave 2,4-(MeO)2C6H3NHC6H4OMe-p, m. 126-7.degree. (Et2O-EtOH), which on nitrosation and redn. by Al amalgam gave 2,4-(MeO)2C6H3N(NH2)C6H4OMe-p.HCl (XVI), m. 136-9.degree.. A soln. of 25 g. XIV and 20 g. AcCH2CHMeCO2Et (XVII) in 250 ml. 2N alc. HCl, refluxed 30 min. after subsidence of the initial reaction, concd. to 80 ml., dild. with 400 ml. H2O, extd. with Et2O, and the dried exts. evapd. and chromatographed on acid-washed Al2O3 in Et2O-petroleum ether gave II (R2 = R3 = Me, R4 = MeO, Y = Et) (IIa), b0.25 150-3.degree., m. 53-5.5.degree. (petroleum ether). Saponification of 13 g. IIa in 200 ml. EtOH by 20 ml. 34% NaOH 6 hrs. under N, diln. with H2O and acidification gave the free acid (IIb), m. 163-5.degree. (aq. EtOH). Other examples of II similarly prepd. were: IIc (R2 = R3 = Me, R4 = Me, Y = Et), m. 88-8.5.degree. (petroleum ether), from 20 g. p-MeC6H4NHNH2.HCl and 20 g. XVII in 250 ml. 2N alc. HCl; IId (R2 = R3 = H, R4 = MeO, Y = Et), from 0.1 mole each of XIV and (MeO)2CHCH2CH2CO2Et; and IIe (R2 = Me, R3 = H, R4 = Cl, Y = Et), m. 85.degree. (petroleum ether), from 0.1 mole each of AcCH2CH2CO2Et and p- ClC6H4NHNH2.HCl in 300 ml. 2N alc. HCl, refluxed 1 hr. AcCH2CHEtCO2Et was treated with XIV to give II (R2 = Me, Y = Et, R4 = MeO) (IIf). Fused ZnCl2 (28 g.) and 10 g. p-O2NC6H4NHN:CMeCH2CHMeCO2H in 20 ml. abs. EtOH were refluxed under N 12 hrs., dild. with 200 ml. 2.5N HCl, and extd. thrice with 200 ml. Et2O. After drying and concn., the exts. were treated 8 hrs. with 200 ml. refluxing 1N alc. HCl, concd. to give II (R2 = R3 = Me, R4 = NO2, Y = Et) (IIg). A mixt. of 50 g. 2,4-Me2C6H3NHCOEt, 50 g. NaNH2, and 500 ml. PhNEt2 was refluxed under N 1 hr., to give 38 g. 2-ethyl-5-methylindole (XVII), m. 72-84.degree. (cyclohexane). Treatment of 4.4 g. XVII with 5.4 ml. 25% aq. Me2NH, 2.25 ml. 40% aq. CH2O, and 3 ml. HOAc 5 hrs. and addn. of 25 ml. 10% KOH gave a gum which was extd. with Et2O. Extn. of the Et2O soln. with 1.25N HCl, neutralization, reextn. with Et2O, drying, and evapn. gave 2.3 g. 2-ethyl-5-methylgramine, m. 100-3.degree. (cyclohexane), 2 g. of which and 4.0 g. KCN in 32 ml. 80% EtOH, refluxed 68 hrs., neutralized with HCl, concd., dild. with 20 ml. H2O containing 2.3 g. KOH, refluxed 6 hrs., acidified and extd. with Et2O gave 1.0 g. II (R2 = Et, R3 = H, R4 = Me, Y = H) (IIh), m. 137-8.degree. (C6H6). Treatment of 13 g. IIa in 75 ml. Me2NCHO with 2.5 g. NaH-mineral oil dispersion in 100 ml. Me2NCHO 1 hr., followed by 8.0 g. o-ClC6H4CH2Cl 14 hrs. gave I(R1 = H, R2 = R3 = Me, R4 = MeO, R5 = 2-Cl, b = 1, M = EtO) (Ia), m. 118-22.degree. (C6H6-Skellysolve B). Saponification of Ia in 125 ml. EtOH by 20 ml. 34% NaOH gave 8.5 g. free acid, m. 191-2.degree. (C6H6). Other examples of I prepd. from IIa by action of NaH and a benzyl halide were those in which the benzyl groups were: m-ClC6H4CH2, and the free acid, m. 191-2.degree. (EtOAc-Skellysolve B); 2,4-Cl2C6H3CH2, m. 130.degree. (aq. EtOH), and the free acid, m. 184-6.degree.; p-MeOC6H4CH2, sirup, and the free acid, m. 153-3.5.degree. (C6H6-petr. ether); p-FC6H4CH2, and the free acid, m. 164-5.degree. (EtOAc-petr. ether); p-HF2CSC6H4CH2, oil from IVa, and the free acid, m. 132-3.degree. (PhMe); p-HF2COC6H4CH2, oil, 20.9 g. from 13.0 g. IIa and 12 g. V, and the free

acid, m. 144-6.degree.; p-ClC6H4CH2, Ib, which was also prepd. from 11.7 g. IIb, 5.0 g. NaH, and 8.8 g. p-ClC6H4CH2Cl, and the free acid, m. 163-5.degree. (C6H6), p-BrC6H4CH2, and the free acid, from p-BrC6H4CH2OSO2Me; p-IC6H4CH2, and the free acid, from p-IC6H4CH2OSO2C6H4Me-p; p-MeSC6H4CH2, Ic, sirup, from VI, and the free acid, m. 170-1.degree. (C6H6-petr. ether); p-(PhCH2S)C6H4CH2, oil from IIa and IX, and the free acid (Id), m. 150-53.degree. (CCl4); p-CF3C6H4CH2, sirup from XI, and the free acid, m. 176-80.degree. (EtOAc- petr. ether); p-NCC6H4CH2, Ie, m. 72.degree. (EtOH), and the free acid, m. 197-200.degree. (EtOAc-petr. ether); p-(Me2NSO2)C6H4CH2, m. 140.degree. (EtOH), from VI, and the free acid, m. 156.5-8.5.degree. (EtOAc-petr. ether); p-EtSC6H4CH2, from VIII, and the free acid, m. 126-33.degree. (2% C6H6 in abs. EtOH); p-PhSC6H4CH2, oil, 42.5 g. from 13.0 g. IIa and 32 g. IX, and the free acid; p-MeSC6H4CHMe and the free acid; and 4-MeS-2-MeC6H3CH2 and the free acid. IIc and p-ClC6H4CH2Cl gave I (R1 = H, R2 = R3 = R4 = Me, R5 = 4-Cl, b = 1, M = EtO) (Ib), m. 89-90.degree., and the free acid (M = OH), m. 185-6.degree.. IIc (24.5 g.) added during 20 min. to 500 ml. Me2NCHO and 6.0 g. NaH, followed by 6.0 g. VII, gave I (R1 = H, R2 = R3 = R4 = Me, R5 = 4-MeS, b = 1, M = EtO), m. 111-13.degree. (Et2O), saponification of 20 g. of which gave 9.6 g. of the free acid, m. 184-7.degree. (ClCH2CH2Cl). From IId were prepd. Et .alpha.-[1-(p-fluorobenzyl)- 5-methoxy-3-indolyl]acetate, and the free acid; and Et .alpha.-[1-(p- chlorobenzyl)-5-methoxy-3-indolyl]acetate, and the free acid, m. 144-8.degree.. IIe and IIf were also converted to their 1-(p-Cl C6H4CH2) derivs. and the corresponding free acids. IIg was converted to I (R1 = H, R2 = R3 = Me, R4 = NO2, R5 = p- MeO, b = 1, M = EtO) (If), which was hydrogenated on Pd-C to the amino compd. (R4 = NH2), from which the Ac, p-ClC6H4CO, and Me2 derivs. were prepd. The corresponding derivs. were prepd. from the free acid obtained by saponificaton of If. Ar-alkylation of 0.05 mole Et .alpha.-(2-methyl-5-methoxy-3-indolyl)-acetate (IIi) with NaH and 0.05 mole p-(PhCH2O)C6H4CH2Cl gave the 1-(p-(PhCH2O)C6H4CH2 deriv., which was saponified to the free acid, hydrogenolysis of which on 10% Pd-C in EtOH gave [1-(p-hydroxybenzyl)-2-methyl-5-methoxy-3-indolyl]acetic acid. Redn. of 18 g. IIi (Y = Me) with 20 g. Sn and 200 ml. 6N HCl under reflux 18 hrs., followed by reesterification with alc. HCl, gave 2.7 g. Et .alpha.-(2-methyl-5-methoxy-2,3-dihydro-3-in- dolyl)acetate, which was aralkylated to prepare the p-ClC6H4CH2, p-MeOC6H4CH2, p-FC6H4CH2, and p-MeSC6H4CH2 derivs., and the hydrochlorides of the corresponding acids. IIa was similarly reduced to the 2,3-dihydro deriv., which was aralkylated to prepare its p-ClC6H4CH2 and p-MeSC6H4CH2 derivs., and the corresponding hydrochlorides. Aralkylation of 9.3 g. IIi (Y = Me) in 50 ml. tetrahydrofuran (THF) with 3 g. NaH in 100 ml. Me2NCHO and 13 g. p-BrC6H4CHBrMe gave I (R1 = R2 = Me, R4 = M = MeO, R5 = p-Br, b = 1) (Ig), and the free acid. From 12.58 g. IIi (Y = Me) was also prepd. 15 g. of the p-Me SC6H4CH2 deriv., sirup, which was hydrolyzed to the free acid, m. 155-6.5.degree. (EtOH); Et ester m. 94-5.degree. (EtOH). Oxidn. of 10 g. Ic (M = EtO) in Et2O by monoperphthalic acid at -25 to -20.degree., chromatography of the crude product on Al2O3, and hydrolysis of the eluted esters gave .alpha.-[1-(p-methylsulfonylbenzyl)-2-methyl-5-methoxy-3-indolyl]propionic acid, m. 194-6.degree. (EtOAc-EtOH-petroleum ether) and .alpha.-[1-(p-methylsulfinylbenzyl)- 2-methyl-5-methoxy-3-indolyl]propionic acid, m. 98-101.degree. (EtOAc-EtOH-petroleum ether). Heating 8.8 g. Ic (M = OH) and 14 g. urea 1.5 hrs. at 190-200.degree. gave the amide (M = NH2), m. 143-4.degree. (C6H6-petroleum ether). A soln. of 24.9 g. Ic (M = OH) and 9.5 g. (+)-PhCHMeNH2 in 350 ml. boiling EtOH was cooled to 20-25.degree. and kept 90 min., giving the (+)-Ic salt of (+)-PhCHMeNH2, m. 170-72.degree. (EtOH), [.alpha.]22D 38.5.degree. (MeOH), which treated with HCl gave (+)-Ic, m. 118.degree. (5:3 Et2O-C6H6), [.alpha.]22D 62.4.degree. (EtOH). Similar treatment of Ib (M = OH) gave the (+)-Ib salt of (+)-PhCHMeNH2, m. 148-9.degree. (Me2CHOH), [.alpha.] 22D 43.degree. (MeOH), and (+)-Ib, m. 156-7.degree. (1:1 C6H6-pet. ether), [.alpha.]22D 60.degree. (EtOH). The filtrates gave (-)-Ib, m.

153-4.degree. (C6H6-petr. ether), [.alpha.]23D-58.degree. (EtOH). Treatment of 31 g. XIIIa and 16 g. XVII in 400 ml. 7.5N alc. HCl gave 13 g. Et .alpha.-[1-(p-chlorobenzyl)-2-methyl-5-methylthio-3-indolyl]propionate, sirup, saponification of which gave the free acid, m. 154-60.degree. (MeCN). Similar prepns. included: Et .alpha.-[1-(p-chlorobenzyl)-2-phenyl-5-methoxy-3-indolyl]acetate, and the free acid, from p-ClC6H4CH2N(NH2)C6H4OMe-p.HCl (XVIII) and PhCOCH2CH2CO2Et; 1-(p-methylthiobenzyl)-2-trifluoromethyl-5-methoxy-3-indolyl-acetic acid, m. 168-72.degree. (C6H6), from p-MeSC6H4N(NH2)C6H4OMe-p.HCl (XIX) and F3CCOCH2CH2CO2H (Brown, et al., CA 55, 1431c); Et .alpha.-[1-(p-nitrobenzyl)-2-methyl-5-methoxy-3-indolyl]propionate (Ih), m. 102-3.degree. (EtOH), from XV and XVlI and the free acid, m. 188-90.degree. (aq. EtOH); Et [1-(p-methylthiobenzyl)-5-methoxy-3-indolyl]acetate, and the free acid, from XIX and HCOCH2CH2CO2Et (XX); 1-(p-chlorobenzyl)-5-methoxy-3-indolyl-2-acetic acid, m. 146-8.degree., from XVIII and XX; Et .alpha.-[1-(p-chlorobenzyl)-2-benzyl-5-methoxy-3-indolyl]propionate, and the free acid, from XVIII and PhCH2COCH2-CHMeCO2Et; Et .alpha.-[1-(2,4-dimethoxybenzyl)-2-methyl-5-methoxy-3-indolyl]propionate, and the free acid, from XVI and XVII; and [1-(p-chlorobenzyl)-2-carboxy-5-methoxy-3-indolyl]acetic acid (Ii), m. 213-18.degree. (aq. Me2NCHO), from XVIII and HO2CCOCH2CH2CO2H. Hydrogenation of 2.85 g. Ih on Ni at 45-50.degree. in 60 ml. EtOH in the presence of 2.4 ml. 37% CH2O and 5 ml. HOAc gave Et .alpha.-[1-(p-dimethylaminobenzyl)-2-methyl-5-methoxy-3-indolyl]propionate, saponification of which gave the free acid, m. 193-4.degree. (MeOH). Hydrogenation of 4.25 g. Ih on 1 g. Pd-C in 100 ml. Ac2O and 100 ml. HOAc gave Et .alpha.-[1-(p-acetamidobenzyl) - 2 - methyl - 5 - methoxy-3-indolyl] propionate. Saponification of 2 g. Ie by 25 ml. 30% NaOH in 150 ml. EtOH under reflux 18 hrs., and acidification by HCl gave .alpha.-[1-(p-carboxybenzyl)-2-methyl-5-methoxy-3-indolyl]propionic acid, m. 230-4.degree. (HOAc or aq. EtOH). Refluxing a soln. of Ii in Ac2O 2 hrs. gave the anhydride of Ii, m. 205-11.degree., which reacted with abs. EtOH in the presence of 1 equiv. NaOEt at 0.degree. to give the Et ester (Ij), m. 214-16.degree. (aq. MeOH). Heating 5 g. Ij under N 80 min. at 225.degree. gave Et [1-(p-chlorobenzyl)-5-methoxy-3-indolyl]acetate, free acid, m. 146-8.degree. (MeCN-C6H6). Action of SOCl2 in C6H6 on Ij gave the acid chloride, which was reduced by LiAlH(OCMe3)3 in THF to Et [1-(p-chlorobenzyl)-2-formyl-5-methoxy-3-indolyl]acetate (Ik). Redn. of Ik by NaBH4 gave the lactone of [1-(p-chlorobenzyl)-2-hydroxymethyl-5-methoxy-3-indolyl]acetic acid, which was treated with PhCH2SK in EtOH to give [1-(p-chlorobenzyl)-2-(benzylthiomethyl)-5-methoxy-3-indolyl]acetic acid. A mixt. of 19 g. (COCl)2 in 25 ml. Et2O and 35.7 g. 1-(p-chlorobenzyl)-2-methyl-5-methoxyindole in 900 ml. Et2O was stirred 2 hrs. and filtered. The solid was added to 660 ml. EtOH and treated with 0.12 mole NaOEt 1 hr., then poured into 660 ml. H2O containing 10 ml. HOAc, giving Et .alpha.- [1-(p-chlorobenzyl)-2 -methyl-5 -methoxy-3 -indolyl] oxoacetate (XXI), m. 113.degree. (C6H6-petr. ether). A mixt. of 36.02 g. MePh3P+Br- and 94.36 ml. 1.10N BuLi in 500 ml. dry Et2O was stirred. 1 hr., and 38 g. XXI in 260 ml. C6H6 and 500 ml. Et2O was added. After 1 hr., the mixt. was heated to 65-70.degree. in a pressure flask 5 hrs. The resulting gum was triturated thrice with 500 ml. portions of 33% C6H6 in Et2O. The dried exts. were concd. to a sirup, which was slurried in C6H6 and chromatographed on Al2O3. Elution with 30% Et2O in pert. ether and evapn. gave Et .alpha.-[1-(p-chlorobenzyl)-2-methyl-5-methoxy-3-indolyl]acrylate (XXII), m. 94-5.degree. (petroleum ether), which was saponified to the free acid, m. 187-8.degree. (EtOH). Treatment of 1.8 g. XXII in 10 ml. THF with 4 g. CH2I2, 1.25 g. Zn-Cu, and 0.2 g. iodine in 20 ml. THF with refluxing under N 20 hrs. gave 1.2 g. Et .alpha.-[1-(p-chlorobenzyl)-2-methyl-5-methoxy-3-indolyl]cyclopropanecarboxylate. The free acid, m. 220-4.degree., was obtained by saponification. The title compds. and their nontoxic salts have anti-inflammatory properties.